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A NEW MICROBODY FOUND IN THE BLOOD IN A CASE OF MYELOGENOUS LEUKEMIA AND THE EFFICACY OF ARSPHENAMIN ON THE DISEASE *

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MUKDEN, SOUTH MANCHURIA

In pathogenesis, chloroma is closely related to leukemia, so that although the former is regarded by some authors as belonging to the malignant tumor group, it is now generally accepted that chloroma is an atypical form of leukemia. It is well known that the exact clinical diagnosis of chloroma is sometimes extremely difficult. In our case it seems probably justifiable to consider the disease as myeloblast-chloroleukemia, but from the clinical point of view, without performing necropsy, we think it may be proper to call it an acute myeloblast-leukemia, with the accompaniment of a chloroma-like tumor in the skull.

REPORT OF CASE

History.—A boy aged 5 years and 9 months, with a negative family history, entered the hospital Dec. 13, 1915. Two years previously, he had had acute nephritis and in the previous May, whooping cough, followed by diphtheria and measles, successively. The onset of the present illness was ten days before admission. At the onset he developed a sudden rise of temperature, with swollen neck and a sore throat. The fever had been continuous to the time of admission. His appetite was poor, his bowels regular.

Physical Examination.—On admission the patient looked like one suffering from scarlet fever of a severe form. His face expressed great anxiety and the breathing was jerky, owing to the swelling of the throat. There was no delirium. The boy was of moderate size, and of slight frame. He was emaciated. The skin showed nothing worth mentioning, neither change in color, eruption, nor desquamation. The development of the subcutaneous fat was poor. The pulse was regular in rhythm, but increased in frequency (130 per minute). Its tension was moderate. His tongue was dry. There was strong *foetor ex ore.* Both tonsils were enlarged and intensely reddened. The pharyngeal mucous membrane was also involved in the congestion, but there was no sign of ulcer or pseudomembrane. The cervical glands on both sides were enlarged to bean size and were painful on pressure. They were hard and firm. No notable change in the viscera of thorax and abdomen could be found. The thymus was not enlarged. The edge of the liver was palpable

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* Submitted for publication May 1, 1918.

* From the Department of Pediatrics, Japanese Medical School Hospital, Mukden, South Manchuria, China.

at the costal margin in the right mammary line. The spleen was not felt. Neither thickening nor aching in the bones were present. The urine was acid in reaction and slightly turbid. Albumin was absent, but the diazo reaction was strongly positive.

Course of the Malady.—The general course of the disease is summarized in the accompanying chart. Therefore, only some clinical findings particularly worthy of mention will be noted.

Dec. 17, 1915. Albumin occurred in the urine in small amount. The diazo reaction was strongly positive. On examination of the urinary deposits microscopically, some leukocytes alone were found. No further change in the pharynx was noted. The swollen glands of the neck increased in number and size. The pharyngeal mucus showed mostly the *Staphylococcus albus.*

December 21. Hematuria occurred. The angina was still severe. Markedly enlarged lymphatic glands of the size of a bean or that of a lentil were counted to the number of nine on each side of the neck. Many other smaller ones were felt also. The glands in the axilla, elbow and groin became involved in the swelling. Many of them were of lentil size.

December 23. Hematuria continued. In the evening the boy had a chill followed by the appearance of many petechia on the front of the left arm. The pharyngeal congestion was markedly diminished. Pallor increased. The upper limit of the liver was situated in the normal position. The lower edge, however, was easily felt 2 cm. below the costal margin in the mammary line. No remarkable change in the character of the edge was detected. The spleen was not palpable.

December 24. The first intramuscular injection of 0.15 gm. neo-arsphenamin was given.

December 26. The hematuria increased. The urinary sediment contained many blood corpuscles and a few casts. The boy's appetite continued poor. No sign of edema was found.

December 28. The congestion of the throat had almost entirely disappeared. The appetite was lost entirely. The liver diminished in size. It was no longer felt.

December 30. Besides blood cells, many hyaline and granular casts were found in the urinary deposits.

Jan. 4, 1916. A second injection of neo-arsphenamin in doses of 0.2 gm. was given intramuscularly.

January 6. Emaciation and paleness were remarkably increased. Hematuria still continued. The patient, however, remained still vigorous. His appetite got better. There was no sore throat. During the previous few days bone-ache in the right leg became pronounced.

January 11. The bone-ache disappeared. Glandular enlargement diminished markedly, so that only a few small glands could be felt. The boy was cheerful. The amount of blood in the urine decreased considerably. A tumor of a cherry size appeared on the frontal bone at the upper margin of the right orbital cavity, so that the eyelid was distended. It had no connection with the eyeball and was of a cartilaginous consistence, with a smooth surface. No pain, either spontaneous or on pressure, was felt.

January 18. The urine contained a trace of albumin, but showed nothing microscopically.

January 20. The urine was normal.

January 22. The orbital neoplasm became further enlarged. No pigmentation was observed either on or through the skin over the tumor. Sight and hearing were not affected. The third intramuscular injection of 0.1 gm. arsphenamin was made.

January 26. The patient was feverish. Some red blood cells and casts occurred in the urine again. The boy was cheerful and had a good appetite. The enlargement of the lymphatic glands had disappeared.

February 1. Although the nutrition was not yet up to normal and the boy still looked pale and sallow, the general improvement was quite noticeable. He felt fine, ate with good appetite and would no longer stay in bed. He was apparently well and left the hospital at his own request.

The results of the blood examination are shown in Table 1.

Treatment.—Arsphenamin (salvarsan brand) was the specific remedy applied throughout the course of the disease, save that the patient was twice (December 22 and 23) put on injections of 10 c.c. of 10 per cent. gelatin, and infusion of uva ursi was tried for the intercurrent hemorrhagic nephritis. No other medicine was given. Milk was the sole food. The amount taken daily was not over a half liter the first few days. Afterward the amount was increased and finally 1.5 liters was the ration.

Further Course of the Disease.—March 4, the boy visited our hospital again. At that time he was looking well. Considerable improvement in his nutrition had taken place in the course of the two months since his discharge. On examination no remarkable change was found in the pharynx, viscera or lymphatic glands. The orbital tumor, however, was further enlarged and had reached the size of a chestnut. The consequence was a lessening of the upward movement of the eyeball. Another tumor had made its appearance on the left temporal bone. It was hemispherical in shape and as large as a hen's egg. It was not mobile. As regards its nature, it was quite similar to that of the orbital tumor. The senses of sight and hearing were normal.

Outcome.—Following this visit we had no further opportunity to see the patient. Later, we learned from his mother that the boy was almost always lively enough to play around and though he was sometimes feverish, the temperature was never over 38 C. The tumor, however, progressively enlarged and his death occurred at the end of April, 1916. The total course of the malady was about five months.

From the foregoing, some clinical signs of peculiar importance may be noted: The continuous fever, the angina, the glandular enlargement, the hemorrhagic nephritis, the strong diazo reaction in urine, the petechia, the marked leukocytosis, with the appearance of the pathologic myelogenous white cells and the tumors on the skull were the chief evidences of the disease.

A NEW MICROBODY FOUND IN THE CIRCULATING BLOOD

A peculiar microbody was found in the blood some time in the course of the disease, which we think is worth while describing. As mentioned, arsphenamin was used three times in the case, which may have given rise to the appearance of the microbodies. They were observed the first time on the third day after the second arsphenamin injection. Ten days later, when the blood films were examined again, the microbodies were no longer to be found. The second appearance took place on the second day after the third arsphenamin administration, this time also lasting for a few days only. The microbodies were found, five to ten in number, in one field of vision of the fresh blood film made in the usual manner, examined with a $\frac{1}{12}$ oil immersion lens and an ocular 3 Leitz.

Form and Structure of the Microbody.—The bodies were examined in fresh blood films only, as we were not successful in getting stained preparations at that time. They were oval in shape and had a distinct contour (Fig. 2). Although they differed slightly in size, the average measures were from 2.5 to 3.0 and 1.5 to 2.0 microns in length and breadth, respectively. The body consisted of two parts—the protoplasm and two nucleus-like corpuscles. The former was a nontransparent, homogeneous mass of grayish-white color and contained neither granules, pigment nor vacuoles. The corpuscles were glistening masses of round shape and of the same size. They were placed one at each pole of the microbody. Flagella were not to be seen. Every one of the microbodies had almost the same structure. They made neither movement nor changed shape. They were always found outside of the blood cells, free in the plasma (see figure). They were resistant to acetic acid of 0.3 per cent. concentration which was used to destroy the erythrocytes to facilitate counting the leukocytes.

None of the experiments for staining, culturing and transmission to animals of the microbodies was successful. It was peculiar that the bodies could never be stained, though the blood cells were found well dyed on the same film.

Nature of the Microbody.—In discussing the nature of these bodies the first thing to be remembered is that the observations were made with fresh blood films alone. In such a condition it is not necessary to differentiate the microbody from an artificial product which may be formed only when complicated manipulation such as fixing or staining is applied to blood films. Moreover, all of these microbodies were similar to each other in both size and structure and were found merely in a certain stage in the course of the disease. In any other state, whether in health or illness, such a structure has never been observed in the human blood. The microbody, therefore, should not be regarded as an artificial product, but is to be considered as specific to the disease concerned.

Varieties or incidental products of the blood cells formed by arsphenamin influences are next to be differentiated. The microbodies contained no hemoglobin and were resistant to dilute acetic acid as mentioned. Every one of them had a similar structure and form. They could never be stained, while the normal as well as the pathologic white cells were well dyed. From these points, it is fair to consider that the microbody is not the incidental product of either erythrocyte or leukocyte. So far as we know, no blood cell body has been described which has such a structure as that of the microbody.

Although Kurloff-Patella's body in the blood of the normal guinea-pig and the large lymphocyte-containing vacuole observed in a case of

TABLE 1.—Blood Findings

Date	Total Erythrocyte Count*	Total Leukocyte Count	Ratio of Leukocytes to Erythrocytes	Hemoglobin†	Color Index	Polychromatophilia	Differential Leukocyte Count in per Cent.									
							Large Lymphocytes	Small Lymphocytes	Large Mononuclears and Transitionals	Myeloblasts	Promyelocytes	Myelocytes	Metamyelocytes	Polymorphonuclear Neutrophils	Polymorphonuclear Eosinophils	Mast Cells
12/13/15	4,072,000	84,610	48	60	0.74	0.7	6.0	12.0	9.0	8.0	5.0	13.0	1.0	44.0	0.7	0.3
							18			27						
12/16/15	3,792,000	88,960	43	60	0.79	0.7	8.0	14.0	4.0	8.5	8.0	14.0	4.5	36.0	0.7	0.3
							22			35						
12/21/15	3,020,000	61,120	49	57	0.94	0	5.0	11.0	8.0	7.5	4.0	19.0	7.5	34.0	0.3	0.7
							16			38						
12/24/15	2,392,000	49,520	48	50	1.01	0.3	5.0	16.0	6.0	4.0	6.0	19.0	2.0	41.0	0.7	0
							21			31						
12/27/15	3,128,000	42,720	73	45	0.72	0.3	2.0	23.0	5.0	3.0	2.0	18.0	5.0	41.0	0.7	0
							25			28						
12/31/15	1,992,000	27,360	73	47	1.18	0	4.0	30.0	8.0	1.5	2.5	14.0	4.0	34.0	1.0	0
							34			22						
1/17/16	1,832,000	10,880	168	38	1.04	0	6.0	45.0	8.0	2.0	2.0	3.5	0.5	32.0	1.0	0
							51			8						
1/24/16	2,544,000	19,040	133	50	0.98	0	8.0	37.0	5.0	3.0	1.5	5.0	0.5	38.0	1.0	0
							45			10						

* Thoma-Zeiss' hemocytometer was used.
† Sahli-Gower's hemoglobinometer was used.

acute leukemia by Pappenheim and Hirschfeld[1] were reported, either of them is nothing but the leukocyte itself. They differ entirely from our microbody either in size, in structure, or in staining properties, so that it is now beyond question that the microbody does not belong to such a varietal form of leukocyte.

Accordingly, it seems to be justifiable at last to consider the microbody as a parasitic organism in the blood. It, indeed, must be a new parasite, because in comparison with the known parasitic protozoa and yeasts, none of them is related to the microbody in any point; and furthermore, Hoefer's,[2] Loewit's,[3] Pappenheim's[1] and Kopanaris'[4] corpuscles are quite different from ours.

The nature of leukemia and the associated diseases is unknown. Some authors regard leukemia as related to the malignant tumor, but there are few adherents to that opinion. On the other hand, the disease, especially its acute form, resembles more an infection, which gives rise to pathologic hyperplasia of the leukoblastic tissues. Various organisms have been described, but nothing specific has been determined. Owing to the consideration, however, that the streptococcus or staphylococcus plays often a certain important part in the etiology of acute leukemia, some authors, such as Sternberg,[5] Pappenheim,[6] Lehndorff,[7] Ziegler and Jochmann[8] and Luedke,[9] regard the disease as being caused by the specific reaction of the hematopoietic tissues against the septicemic process in a certain individual constitution, and subsequently they suggest that it is not necessary to have to determine a specific virus for the genesis of leukemia.

Although our microbody is probably a new parasite and may have a certain etiologic meaning as discussed in the foregoing, we do not yet insist on regarding this body as the sole causative factor of the disease. Nevertheless, we think it is proper to consider that this parasite acts as an exciting cause of the disease, the essential part of the etiology being existent in the peculiar disposition of the hematopoietic system.

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1. Pappenheim and Hirschfeld: Folia haemat., 1908, **5,** 361.

2. Hoefer, P. A.: Centralbl. f. Bakt. u. Parasitenk., Orig., 1910, **55,** 19.

3. Loewit, M.: Die Leukaemie als Protozoeninfektion, Wiesbaden, 1900; Ztschr. f. Heilk., Abt. f. path. Anat., 1900, **21,** 280; Ibid., 1901, **22**; Ziegler's Beitr. z. path Anat. u. z. allg Path., 1903, **33,** 113; Centralbl. f. Bakt. u. Parasitenk., Orig., 1908, **45,** 600.

4. Kopanaris: Arch. f. Schiffs- u. Tropen-Hyg., **16,** 313.

5. Sternberg, K.: Wien. klin Wchnschr., 1911, No. 47.

6. Doehrer and Pappenheim: Folia haemat., 1913, **16,** 145; Pappenheim and Hirschfeld: Ibid., p. 368; Pappenheim: Ztschr. f. exper. Path. u. Therap., 1914, **15,** 39.

7. Lehndorff, H.: Jahrb. f. Kinderh., 1910, **72,** 53.

8. Ziegler and Jochmann: Deutsch. med. Wchnschr., 1907, No. 19, p. 749.

9. Luedke, H.: Deutsch. Arch. f. klin. Med., 1910, **100,** 553.

EFFICACY OF ARSPHENAMIN ON ACUTE MYELOGENOUS LEUKEMIA

Arsphenamin has been employed in the treatment of chronic leukemia by several authors, but the effect has not been striking in any case, except that of Ireland,[10] who claimed to have obtained some improvement of the disease through the remedy. As regards the influence of arsphenamin on an acute form of leukemia, no report suggesting its curative value has ever been published.

Using arsphenamin in our case of acute myelogenous leukemia, a marked apparent recovery was observed both in the general and the local symptoms. The patient, who looked like one suffering from a severe form of scarlet fever on admission, got three successive injections of the remedy which, as noticed elsewhere, was the sole specific treatment employed in the case. The effects were so remarkable that the fever, which had been as high as 39 C., made a gradual decline to the subfebrile point, the appetite returned and the boy became lively again. Furthermore, the hemorrhagic nephritis was cured, the diazo reaction disappeared and the subcutaneous bleeding also ceased. The swelling and the injection of the pharyngeal mucous membrane were gone, so that difficulty in swallowing and breathing disappeared and the soreness in the throat was no longer felt. The enlarged lymphatic glands became reduced markedly in size. Thus, all of the acute symptoms of the disease were almost perfectly dissipated by the arsphenamin.

The efficacy of arsphenamin in leukemia is to be demonstrated more directly in the change of the blood constitution. As regards our case, a remarkable improvement, not only in quantity, but also of quality, occurred in the state of the colorless corpuscles. The total number was decreased from 80,000 to 10,000. The young type of leukocytes, which had been ranging from 27 to 38 per cent. before treatment, were reduced gradually in number to reach, finally, 8 to 10 per cent. of the total leukocytes. Accordingly, the blood picture more closely approached that of the normal state. Although it was not possible to drive all of the pathologic leukocytes out of the blood current, and some of them were left, these were so few that they scarcely made up more than one-twelfth to one-thirty-fifth of the initial count. On the contrary, the lymphocytes were increased from 18 per cent. to 45 per cent. The latter figure approximates the normal standard of this kind of white cells at the age of the boy referred to. The differential count of the physiologic granulocytes also became normal.

It is therefore to be concluded that arsphenamin produced the most noticeable influence in a curative sense on the white cells. As regards

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10. Ireland, Baetjer and Ruhräh: Jour. Am. Med. Assn., 1915, **65**, 948.

the red blood cells, they were greatly lessened. This quantitative diminution, however, should not be considered as indicating an aggravation of the leukemic process. The anemia occurring in the course of leukemia is usually regarded as due to the diminishing productive function of the erythroblastic tissue, which is induced by an excessive proliferation of the leukoblastic elements of the blood-making organs.

As to the cause of the pallor in our case, however, such an explanation as the foregoing is not to be applied, for the changes brought about in the state of the colorless corpuscles suggested that the hyperplastic process which had been raging in the leukoblastic tissue was no longer in progress, or it was, rather, diminished through the treatment. The actual etiologic factor of moment, therefore, was to be found in the serious bleedings themselves which came on in the course of the disease. Besides the complication of nephritis, the diminished erythroblastic function as a result of the general weakness caused by the nutritive deficiency due to the long continuance of the sole milk diet and the intensified destructive process of the red blood cells as a general phenomenon in the course of a febrile disease, were also to be considered to have played important parts in inducing anemia in our case.

Notwithstanding the therapeutic use of arsphenamin, which resulted in the disappearance of most of the symptoms of the disease, the tumor growths occurred in the skull, as mentioned in the history. On account of this, however, the curative value of the remedy should not be doubted.

Recovery in leukemia and chloroma is practically unknown. The cases reported by Tuerk[11] and by Luedke,[9] in which they claimed to have observed a certain recovery, belong to the exceptions. Although a curious remission may occur spontaneously in leukemia, the acute form of the disease runs a malignant course steadily, to reach a fatal outcome in a short time. Accordingly, the marked improvement extending over a considerable period, and, developing soon after the application of arsphenamin, as in our case, should not be regarded as being produced by the influence of the remedy.

Occasionally the disappearance of some of the leukemic symptoms may occur when septicemia comes on in the course of the malady. In such a case, however, owing to the complication itself, the general condition of the patient becomes worse and early death ensues, so that any remission can never be observed.

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[11] Tuerk: Wien. med. Wchnschr., 1907, p. 939.

MODE OF ACTION OF ARSPHENAMIN ON THE DISEASE IN INDUCING THE DIMINUTION OF LEUKOCYTES

From the foregoing it is evident that the influence of arsphenamin was most remarkable in improving the state of the colorless corpuscles. It now remains to discuss the mode of action of the remedy in causing this hematologic change. The lessening of the leukocytic count may be brought about in one of the following ways:

Uneven distribution of leukocytes in the body, which occurs while the majority are retained in some of the inner organs and the remainder only are left free in the blood current, may be the cause of the lower count of the cells in the peripheral blood vessels. That this is not true is shown by the fact that there is no evidence of a similar process in any other disease under treatment with arsphenamin, and also by the fact that arsphenamin undergoes steady excretion from the time it is introduced and is not kept in the body in such a sufficient quantity as to exhibit its activity continuously for such a long period as occurred in our case; and moreover, the marked relief of various other symptoms does not suggest the justifiability of such an explanation. The diminution of the leukocyte count, therefore, is to be regarded as a result of an actual decrease in number in the whole circulatory system and not of their uneven distribution in the body.

The change in the blood picture may be induced by an abnormally increased activity of the leukocytolytic process. But that this was not the case is proved by the result of the investigation of the purin metabolism. Applying the method of Hopkins-Woerner, the routine analysis of the urine regarding uric acid was carried out. The patient was fed on a purin-free diet — milk alone — with the purpose of estimating the endogenous purin excretion. The chart and Table 2 show the result of the analyses. Uric acid is estimated in amount of excretion in twenty-four hours.

In the acute and malignant stage, in the early course of the disease, uric acid was estimated at the amount of not exceeding 0.279 gm. per day. Later, even when the transitory recovery from the disease as the result of the arsphenamin injections and the lessening of leukocytes occurred, the excretion of uric acid was not increased, but reduced to such a small amount as less than 0.05 gm. This shows that the destruction of leukocytes was not beyond the normal, or rather was decreased.

The same conclusion may be made from the hematologic point of view. If the leukocytolytic process be active in an organism, the consequence is the appearance of the young types of the white cells in a considerable number in the blood current, provided the hematopoietic function is kept in maintenance. On the contrary, in our case, the

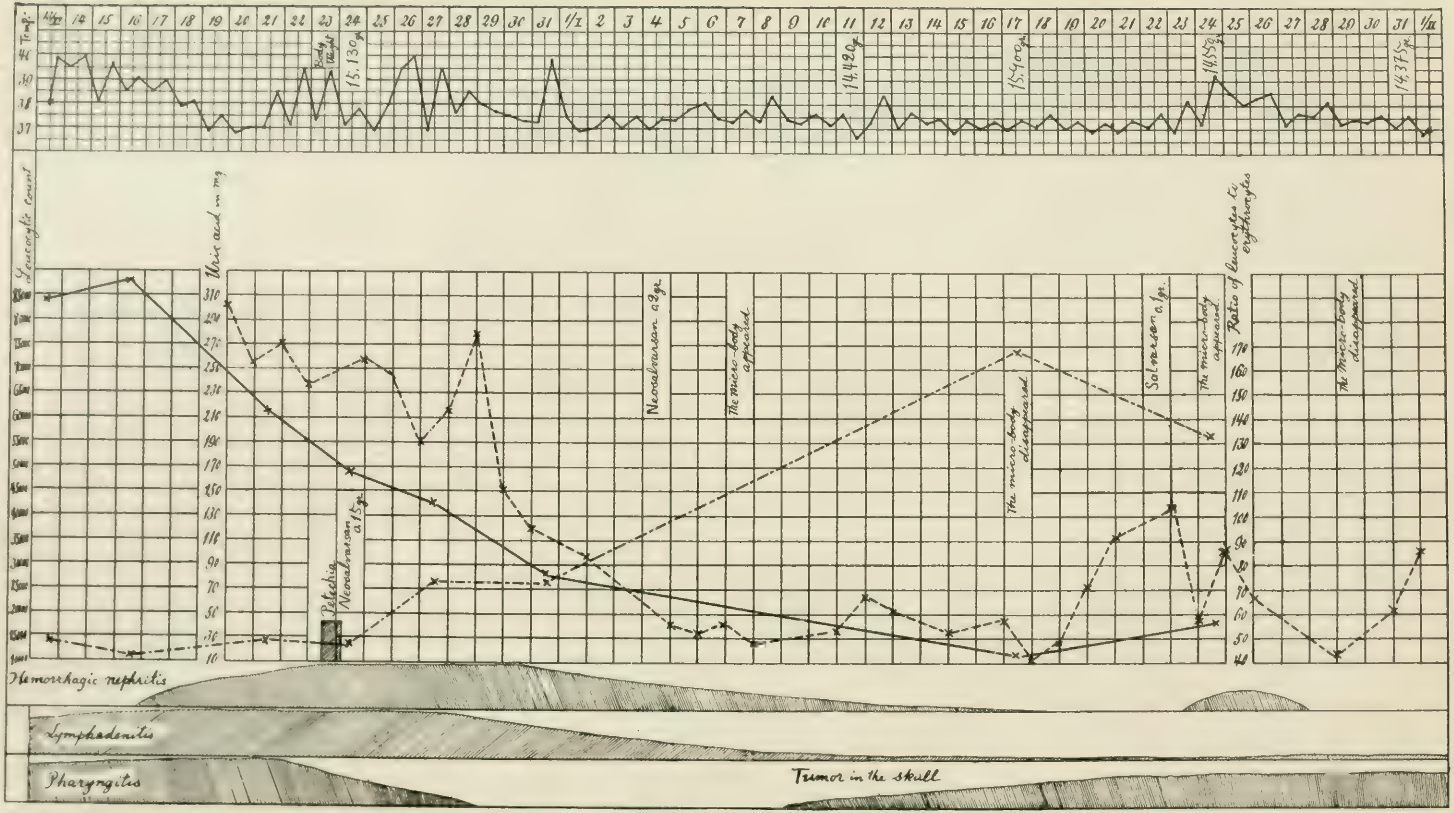

Fig. 1.—Diagram showing the chief symptoms, the blood findings and the amount of uric acid excreted. ——— leukocytes; —.—.—.— ratio of leukocytes to erythrocytes; — — — — amount of uric acid.

TABLE 2.—URINE

Date	Amount in C.c.	Specific Gravity	Albumin	Deposits				Uric Acid in Mg
				Erythrocytes	Leukocytes	Tube Casts	Epithelium	
12/19/15	590	1.008	±	—	—	—	—	297
12/20/15	400	1.009	±		—	—	—	[illegible]
12/21/15	490	1.011	+++	+++	+	—	—	270
12/22/15	460	1.011	+++	+++	+	++*	—	233
12/23/15	1,040	1.006	+++	+++	+	++*	—	250
12/24/15	500	1.004	+++	+++	+	++*	—	254
12/25/15	410	1.015	+++	+++	+	++*	—	245
12/26/15	280	1.010	+++	+++	+	++*	—	190
12/27/15	300	1.015	+++	+++	+	++*	—	213
12/28/15	750	1.012	+++	+++	+	++*	—	277
12/29/15	420	1.017	+++	+++	+	++*	—	150
12/30/15	680	1.013	+++	+++	+	++*	—	120
12/31/15	...	.....	......	......	......	......	......	...
1/ 1/16	830	1.009	+++	......	......	......	......	95
1/ 2/16	470	1.014	+++	......	......	......	......	176
1/ 3/16	960	1.011	+++	++	—	++*	—	...
1/ 4/16	820	1.011	+++	++	—	++*	—	37
1/ 5/16	840	1.010	+++	++	—	++*	—	35
1/ 6/16	870	1.010	+++	++	—	++*	—	44
1/ 7/16	810	1.011	+++	++	—	++*	—	25
1/ 8/16	860	1.014	++	......	......	......	......	...
1/ 9/16	690	1.014	++	......	......	......	......	...
1/10/16	980	1.007	++		++	++	—	33
1/11/16	1,155	1.007	++	—	++	++	—	65
1/12/16	950	1.009	++	......	......	......	......	53
1/13/16	920	1.010	+	......	......	......	......	...
1/14/16	730	1.008	+	......	......	......	......	43
1/15/16	770	1.010	±	......	......	......	......	35
1/16/16	810	1.010	±	—	+	—	—	45
1/17/16	830	1.007	±	—	—	—	—	15
1/18/16	840	1.008	—	—	—	—	—	24
1/19/16	730	1.010	—	......	......	......	......	74
1/20/16	840	1.008	—	......	......	......	......	113
1/21/16	860	1.009	—	......	......	......	......	...
1/22/16	900	1.009	—	......	......	......	......	135
1/23/16	830	1.008	—	......	......	......	......	42
1/24/16	840	1.008	+	......	......	......	......	103
1/25/16	820	1.008	+	......	......	......	......	66
1/26/16	1,100	1.007	+	+	—	±	—	...
1/27/16	710	1.008	+	......	......	......	......	...
1/28/16	790	1.008	—	—	—	—	—	17
1/29/16	920	1.007	—	......	......	......	......	...
1/30/16	1,010	1.008	—	......	......	......	......	54
1/31/16	760	1.008	—	......	......	......	......	104

* Granular.

count of the young types of leukocytes became less, in spite of there being no decrease of the blood-making activity in the tissues, as is suggested by the leukocytic picture.

Accordingly, it is most probable that the striking improvement of leukocytes, both in form and number, is due to the inhibition of the leukoblastic function, especially of the myelogenous white cells, which is caused either through the direct influence of arsphenamin on the hematopoietic organs, or indirectly as a result of the primary germicidal action of the remedy.

SUMMARY

A case is reported of acute myeloblastic leukemia accompanied by chloroma-like tumor growths in the skull, occurring in the course of the disease.

Arsphenamin was used in three injections, which resulted in an astonishingly good effect in causing the cessation of all of the leukemic symptoms, with the exception of the gradual enlargement of the tumors. The improvement in the blood findings was very remarkable.

In consequence of the arsphenamin treatment, a great number of peculiar microbodies made their appearance in the blood. The nature of these bodies was not determined, but it is considered justifiable to regard them as a new variety of parasitic micro-organism of a certain pathogenic significance in this case of leukemia.

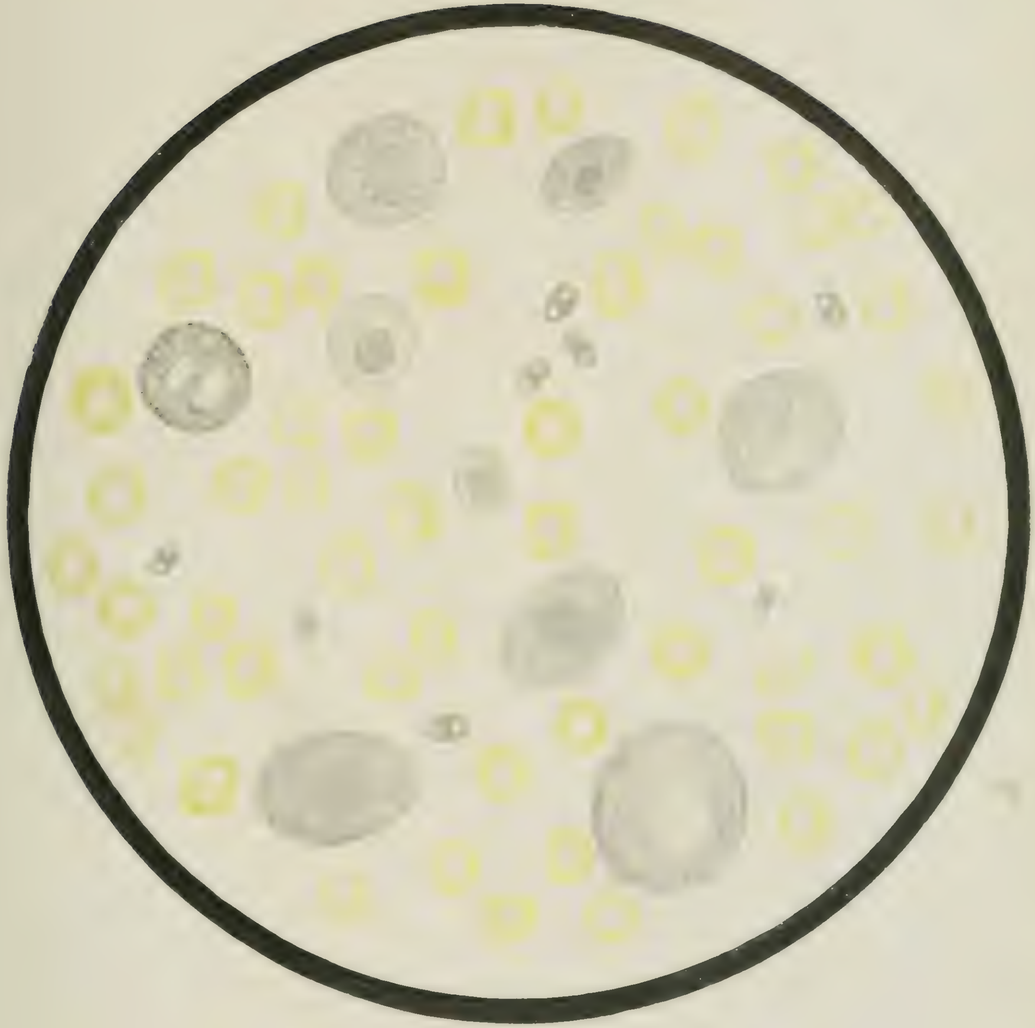

Fig. 2. Blood film preparation showing the new microbodies

Illustrating Article by Itsuyoshi Inada, M.D., and Shun Ohashi
American Journal Diseases of Children, July, 1918.

A CLINICAL CONSIDERATION OF MACEWEN'S SIGN

ESPECIALLY WITH REFERENCE TO ITS USE IN POLIOMYELITIS *

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In a previous article[1] on the hydrocephalus of poliomyelitis we frequently referred to Macewen's sign and endeavored to emphasize its importance in the detection of this condition. The great clinical importance of the sign, its ever widening field of applicability, its relative certainty as an index of the existence of acute hydrocephalus, the simplicity of the methods for its detection and the absence of any detailed description of it in our present day treatises on physical diagnosis were the incentives to the writing of the present paper. The classical description of Macewen will be first summarized, the later study of the subject by Wilcox will be reviewed, and an endeavor will be made further to establish the value of the sign in physical diagnosis.

Macewen of Edinburgh first described the sign. He employed it in the diagnosis of brain tumor and abscess over a period of ten years and found it distinctly useful. Quoting more or less directly from his original description,[2] he says:

The percussion note is produced by the vibration of the cranial walls when struck and is modified by the consistency and the volume of the contents and their relative position to the bone. When struck a thin skull vibrates more readily than a thick one; indeed, a skull may be so thick that it vibrates little if at all to ordinary digital percussion. The note obtained in healthy adults is generally high pitched, imparting the idea of solidity; in many adults, in fact, the bones of the cranium are too thick and dense to permit active vibrations. In the cranium of a normal infant, whose bones are only united by membranes, the sound obtained is so dull and flat as scarcely to be perceptible. Should the contents of such a cranium, however, increase sufficiently to produce tension the note becomes clear. In healthy children, in whom the ordinary density, consistency, and relation of healthy brain to the

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* From the Kingston Avenue Contagious Disease Hospital, Department of Health, New York City.

* Read before the Pediatric Section of the Kings County Medical Society, Oct. 22, 1917.

[1] Regan, J. G.: The Hydrocephalus of Poliomyelitis, Am. Jour. Dis. Child., 1918, **15,** 259.

[2] Macewen, W.: Pyogenic Infective Diseases of the Brain and Spinal Cord, Glasgow, 1893, p. 146.

cranial bones exist, a dull note is produced on percussion, but where the contents are more fluid the bones will vibrate more readily and a clearer percussion note will be obtained. A somewhat clear note is sometimes encountered in children who have the typical enlarged head associated with infantile rickets, but the change in note is not constant, and some of these rachitic children with a positive sign have been afterwards proved to have ventricles distended with fluid. When the lateral ventricles are distended with fluid the percussion note is markedly altered, the resonance being greatly increased. The exact musical quality of the note is difficult to describe, but it conveys the idea of hollowness. Macewen further says that he observed to a conclusion ten cases with a positive sign during life, in whom frozen transverse sections of the brain were made post mortem, all showing distended ventricles, with thinning of the brain substance. He considered the upright position most suitable for eliciting the sign, and for percussion employed either the tip of the middle finger or the ordinary instruments used in percussing the chest. He believes the pterion or a little posterior to that point to be the best place to elicit the sign. He also makes mention of the fact that the ear of the investigator may be placed in contact with the head of the patient and the note determined in this manner. Special emphasis is placed on the change in the percussion note at one particular spot according to the position of the patient's head. In most cases the eliciting of the percussion note did not seem to incommode the patients and in many instances the children were amused. The sign was present in forty children and young adolescents having distended ventricles arising from many different causes.

The original description of Macewen was later partly reviewed by Wilcox in an article[3] in which he undertook the difficult task of giving some of the basic principles underlying the question of skull percussion. At the same time he described a new auscultatory percussion method for eliciting the sign. This method consisted of the application of the stethoscope to the forehead just above the base of the nose, after which the skull is tapped directly over the parietal region, beginning over the parietal boss and progressively approaching the point at which the stethoscope is applied. This should be carried out on both sides of the head. The typical sign consists in a high-pitched, short, cracked-pot note. It is most distinct when percussion is being performed over, behind or below the parietal boss, is unchanged as the point percussed passes downward, and diminishes in intensity and character as the percussing finger approaches the stethoscope. The reverse of this occurs when percussing the normal skull, owing to the fact that normally vibrations are better conducted along the bony wall than through the brain and meninges.

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[3] Wilcox, H. B.: Arch. Pediat., December, 1915, p. 909.

Wilcox noted the presence of a positive Macewen sign in children with serous meningitis complicating gastro-intestinal disturbances, pneumonia, typhoid fever and influenza; also in various acute infections of the meninges, especially tuberculous meningitis and poliomyelitis. He found it to be absent in congenital hydrocephalus. He remarked the reduction in the intensity of the sign which may follow lumbar puncture with the removal of varying quantities of spinal fluid, and he considered the sign of value in estimating the necessity for repeated rachiocentesis.

Heiman and Feldstein[4] and Sophian[5] make frequent reference to the presence of Macewen's sign in cases of meningococcus meningitis, the former authors noting it in thirty-five out of forty-five of their patients who were over 2 years of age. Koplik also draws attention to its use in tuberculous[6] and epidemic meningitis,[7] noting it in thirty-four of fifty-two cases of the former disease, and stating that it may appear comparatively early. Neal and Du Bois[8] in a varied and extensive experience with meningeal conditions lay emphasis on the fact that whenever they have found the Macewen sign they have always obtained increased fluid, except in cases of postbasic meningitis.

There is no doubt that the authorities cited have had exceptional opportunity to observe cases in which the value of this sign could be carefully judged, and they all uniformly agree on its decided clinical importance; yet there has been for some time, and there still remains, a general skepticism among a great many members of the medical profession regarding it. This is due in some instances to lack of opportunity to make use of the sign in a sufficiently large number of suitable cases at one time, and no doubt also to the fact that there is at present no true classification of skull percussion.

In order to explain the basis for the existence of the sign in poliomyelitis the gross pathologic picture of the changes in the brain which occur in that disease must be considered. As explained in the aforementioned article[1] under the pathology of the edema of poliomyelitis, the lateral ventricles are often definitely enlarged post mortem. During the early, acute stage of the malady this enlargement is due to distention as a result of the increased formation, diminished excretion and resultant accumulation of the cerebrospinal fluid. The soft, yielding tissue of the cerebral hemisphere is thus compressed between the unyielding calvarium and the distended ventricles. This gives an entirely different relation to the tissues within the cranial cavity, passing from without inwards, as compared with that which exists under normal conditions. Normally on cross section through the skull we should expect to find first the cranium, beneath this and intimately attached to it the dura mater, then the subdural space, then the arachnoid, and beyond this the subarachnoid space, and finally the pia mater closely investing the surface of the brain. The subarachnoid space contains connective tissue trabeculi and a quantity of cerebrospinal fluid, and while not large, yet it is a definite area, and is of a sufficient size to keep the surface of the cerebrum from coming into close contact with the arachnoid, and hence indirectly with the dura and calvarium (the subdural space being usually so small as to be negligible, and the arachnoid and dura lying almost in contact). With the distention of the ventricles and the edematous swelling of the brain tissue that occur with the onset of poliomyelitis, the subarachnoid space is partially, or more usually completely, obliterated—the spinal fluid being displaced into the larger cisternas—the membranes are crowded together, the brain is brought into more or less immediate contact with its bony covering, and the tension of the contents of the cranial cavity is raised.

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[4] Heiman, H., and Feldstein, S.: Meningococcus Meningitis, New York, 1913, p. 138.

[5] Sophian, A.: Epidemic Cerebrospinal Meningitis, St. Louis, 1913, p. 59, 70, etc.

[6] Koplik, H.: Quoted by Brown, in Osler and McCrae's System of Medicine, New York and Philadelphia, 1913, **1,** 423.

[7] Koplik, H.: Med. Rec., New York, 1906, **70,** 481.

[8] Neal, J., and Du Bois, P.: Am. Jour. Dis. Child., 1915, **9,** 1.

It is a recognized fact that in percussion of the lungs when the tension of the pulmonary tissue increases, the resonance becomes more marked. So it is with percussion of the skull—the greater the tension of the cranial contents the more resonant is the quality imparted to the note. Under normal conditions, with the relation of the cerebral contents as previously described, the sound obtained in the frontal and parietal regions is of a dull character and closely resembles that produced by tapping on a thick and not too resonant board. It is a somewhat similar sound to that heard on percussion of any bony surface (except that it is not quite so flat), and is very little influenced by the cranial contents. When analyzed into its component parts it is found to be of high pitch, short duration, slight intensity and resonance. With the increase in intracranial tension, however, the brain closely crowded against its bony envelope, the subarachnoid and the subdural spaces practically abolished, the percussion note becomes decidedly changed in its quality, the vibrations set up in the bone now being easily and directly transmissible to the underlying tissues, giving origin to a new sound. As is the case in pulmonary percussion, this note is of a more resonant character and of a greater intensity, longer duration, but of a lower pitch than the normal note just described. The quality of the sound may be best described, as was done originally by Macewen, by saying that "it conveys the idea of hollowness." Sometimes also it gives the impression of fluid, the more so the younger the child. It is an entirely different sound to that obtained on percussion of any other part of the body. It is best imitated by loosely clasping the fingers with the palmar surfaces opposite but not touching, and then quickly bringing the latter together with moderate force. Some of its qualities are also manifest when forcible percussion is made over a pulmonary cavity with the mouth open.

As we would expect, hydrocephalus may be of various degrees and thus the same sound would not be obtained over a skull in which the ventricles were only slightly distended, and the subarachnoid space only partially obliterated as when the ventricles were markedly distended and the cerebral hemispheres compressed against the bone. In the former instance the note would only be slightly influenced by the cranial contents, while in the latter it would be markedly so. Hence there may be said to be varying degrees of the positive Macewen. Arbitrarily it is best to divide the sign into slight, moderate and markedly positive. The last being identical with the typical sound already described, and the first of a slightly lower pitch, but greater resonance, as well as longer duration than the normal skull percussion note; a moderately positive sign attains a medium between the two.

In recognizing the positive sign, two elements must be considered, namely, the auditory and the tactile. The auditory quality we have just described; but the tactile element is also of importance in the proper interpretation of the sound produced, for there is almost as much change conveyed to the finger on tapping the skull as there is in the sound heard by the ear. It is truly difficult to describe this tactile element because we have no means of dividing it into its various characteristics as we have in the case of sound. There is an appreciable change, however, which the finger by practice will learn to detect. Normally on percussing the skull the impression the finger receives is of a hard, bony, nonresonant, resistant, and unyielding surface, the retention of the vibrations by the bony envelope of the skull being definitely appreciated. With the ventricles distended with fluid, the impression conveyed is distinctly different, in that the vibrations set up are felt to be transmissible to the contained tissues, and the percussed surface feels less resistant and unyielding than previously. This element of the sign is more appreciable in young children than in adults, or adolescents, and, in fact, in the latter two it is usually entirely lacking, owing to the thickness of the calvarium. We believe it is principally the presence of this tactile element in the former class of patients and its absence in the latter which makes Macewen's sign so much more valuable in children.

In eliciting the sign in the routine physical examination of patients with poliomyelitis—and this applies to any other acute meningeal condition as well—we have made use of Macewen's original method, with the exception that of necessity we have employed the recumbent posture, owing to the pain usually produced by any attempt to have the patient sit up during the early, acute stage of the disease. This position has, however, proved perfectly satisfactory in every respect. The method used has been as follows:

The pillow is removed from under the child so that the head lies on an even surface; the head is turned first to one side and percussion is carried on over the region of the parietal eminence which is lowermost, after which the position of the head is reversed and a similar area on the opposite side is percussed. It is often preferable to remove the child from the crib and lay it on a wooden table with a thin pillowslip folded beneath the occiput. It is essential that the room in which the examination is made be quiet, and that the examiner, by bending, bring his ear close to the child's head while the percussion is being carried out. Gentle tapping with the tip of the middle finger is just as effective in bringing out the note as hard loud blows with the finger or a percussion hammer. The use of the latter instrument is open to the decided objection that it prevents the determination of the tactile quality of the sign.

The pterion was the point originally specified by Macewen for best eliciting the sign. We have also used this area in a great many cases, but by comparison have found that the regions of the parietal eminences are just as suitable, if not more so, especially, since the parietal bone in that location is not covered by muscular tissue. In order to facilitate the determination of the degree of the positive sign it is often useful to percuss the skull from behind forward, starting at the lambdoid suture and ending just behind the frontal eminence, following a line which would be just superior to the upper temporal ridge and which passes through the parietal boss. If a marked Macewen's sign is present the typical sound will usually be elicited over most of the entire area percussed; with a moderate or slightly positive sign, the sound will be proportionately more localized to the parietal eminences or to the pterion.

The percussion-auscultatory method of Wilcox has been employed often in our cases, but mostly in a confirmatory way when the sound obtained on percussion is of an indefinite character. In children we have not found it as reliable as the original method, lacking as it does the tactile element. In adolescents and adults it is probably of more value, as percussion often shows very little or no change of note in these patients, owing to the thickness of the cranial walls despite the fact that symptoms of distinct hydrocephalus exist. It is difficult to state just how much more accurate the method of Wilcox is in such cases without a more extended study, but we believe that it may often be found to be distinctly superior. In these older patients, also, it is necessary to emphasize the fact that Macewen's sign must not be relied on too strictly as an index for the treatment of hydrocephalus by rachiocentesis. The other symptoms must here be taken into consideration. Thus, an elevated temperature, rigidity of the neck or limbs, hyperesthesia, drowsiness or stupor, rapid pulse, dilated pupils, sweating, and irregular vasomotor, flushings of the skin, and, if possible, the findings on the examination of the eyegrounds should be the guiding factors rather than the apparent presence or absence of Macewen's sign.

A few factors may slightly interfere with the test even in children. Thus, in the case of colored patients we have often found it relatively unreliable, due no doubt to the frequency of rickets in that race. Then again, a large growth of hair renders difficult direct percussion of the skull and the sound obtained is materially changed. This is simply remedied by clipping the hair, or, if necessary, shaving the scalp. Diseases of the bones, especially rickets, as Macewen and Wilcox have remarked, may falsely simulate a positive sign. Thus various factors must be considered which will cause some deviation from the normal note without there necessarily being a hydrocephalus present. Allowance can usually be made for them, however, as they are readily recognized and rarely interfere to such a serious extent as entirely to disguise or simulate a marked Macewen's sign.

During the 1916 epidemic of poliomyelitis we had ample opportunity to use this sign and to test carefully its value in 1,798 cases in the hospital. We could not help but be impressed by its importance, affording, as it does, a definite physical sign by means of which a diagnosis based on the other symptoms of suspected hydrocephalus may be confirmed and treatment by lumbar puncture instituted. We wish to emphasize its nearly constant value in this particular regard, because at present lumbar puncture would seem to be one of the most important procedures in the treatment of this disease. It is probably encountered more frequently in poliomyelitis, and is more marked than in any other acute disease with the exception of tuberculous meningitis. It is this common occurrence that makes its use in the physical examination of a patient with the former disease of vital importance. Macewen's sign was present in all cases seen in the preparalytic stage of the malady, and was usually of a marked degree. It was also extremely frequent in the early paralytic period of the disease, being present to some extent in over 80 per cent. of the patients, and in some cases, especially of the respiratory type, it persisted for as long as from three to eight weeks after the onset.

The degree of the positive sign was usually proportionate to the pressure and quantity of spinal fluid removed on lumbar puncture. Unfortunately, as spinal fluid pressures were not taken on the cases in which this was noted, and since the estimations of pressure were based on the rate of flow through the needle in a given period of time, the first fact cannot be scientifically proved, yet the clinical impression received by the rough method of estimation used was that a distinct relationship existed, as is shown in the accompanying table. Thus, if Macewen's sign was marked, the fluid was usually under marked pressure, spurting from the needle as soon as the stilet was withdrawn, while if it was slight the fluid would merely flow away rapidly. The relation between the positive sign and the quantity of fluid removed was more easily proved as the table referred to shows.

Wilcox noted a change in the percussion note after the removal of various amounts of spinal fluid. This is what would be looked for if the quantity withdrawn were sufficiently large. It seems hardly likely, however, that the removal of a small amount, say from 5 to 10 c.c., would materially influence the sound; but when larger quantities, from 20 to 30 c.c. or over, are withdrawn, the rate of normal flow (20 drops per minute) being approximated before the needle is withdrawn, the relative position of the contents of the cranial cavity to the bone may be affected to such an extent that a change in the tissue conduction would result and a different note be obtained. This change has been observed very often in our cases following rachiocentesis. The table shows the relation between the positive sign before and after puncture, and the quantity of fluid removed. It demonstrates also that, while a definite relationship exists between all these various factors—of pressure and quantity of spinal fluid, on the one hand, and the degree of the positive Macewen with subsequent change following puncture, on the other—this relation is not of a constant character, for exceptions are not infrequent. The probable explanation of these variations to the rule is attempted in the footnotes at the end of the table.

It is important to remember that a bulging anterior fontanel in an infant has the same significance as a positive Macewen's sign. Many authors consider that the sign is never present if the fontanel is protruding. This does not hold true so far as we could determine for the hydrocephalus of poliomyelitis, nor for that of tuberculous meningitis, and we feel that there is grave reason to doubt it in ventricular distention from other causes. It seems to us it is merely a matter of what a positive Macewen's sign is considered by the individual writer to be. If only the typical note be considered as a Macewen sign, then truly it is rarely present in infants with a bulging fontanel; but we believe that the sound often elicited in cases of extreme hydrocephalus, in which the fontanel is still patent and bulging, is also a Macewen in the true sense of the word, because it indicates a condition of hydrocephalus just as definitely as does the protrusion of the opening. The sound obtained in these cases differs from the typical note, in that it is of a higher pitch, lower resonance and shorter duration, and in that the tactile element is more prominent and more diagnostic. That a Macewen may exist at the same time as a protruding anterior fontanel is certainly a reasonable supposition when consideration is given to the fact that a moderate degree of ventricular distention may produce a tense and bulging opening, while a greater degree will also alter the relation between the cranial bone and its contents, crowding the latter

MACEWEN'S SIGN TABLE OF AUTHOR'S CASES

Case Number	Date Admitted to Hospital	Age, Years	Date of Puncture	Amount of C. S. Fluid, C.C.	Pressure of C. S. Fluid	Degree of Positive Macewen's Sign	
						Before Puncture	After Puncture
2797*	8/18	2	8/20	28	Moderate increase	Absent	Absent
1867	7/26	2½	8/1 8/3 8/4 8/10	30 35 40 35	Marked Moderate Marked Moderate	Moderate Moderate Marked Moderate	Moderate Moderate Moderate Slight
1756	7/22	4	7/24	32	Moderate	Moderate	Slight
2210	8/5	1½	8/12	35	Moderate	Marked	Moderate
2783*	8/18	1½	8/18	20	Not given	Slight	No alteration
2790*	8/18	5	8/18	15	Normal	Slight !	No alteration
3088	9/5	7	9/5	26	Slight	Moderate	Slight
2733	8/16	2	8/18	40	Marked	Marked	Moderate
2858*	8/20	2	8/21	15	Slight increase	Slight	Slight change, hardly noticeable
2655	8/15	2	8/17	25	Slight to moderate increase	Slight to moderate	Slight
2710*	8/16	5	8/16	15	Slight increase	Marked	Marked
2909	8/23	1⅓	8/23	34	Marked increase	Marked	Moderate to slight
1869	7/26	7/12	7/29	38	Marked increase	Bulging anterior fontanel moderate	Fontanel tense but not bulging; Macewen absent
3132	9/12	4	9/12	32	Moderate increase	Moderate	Moderate to slight
2745	8/17	3	8/19	40	Marked	Marked	Moderate to slight
2963	8/28	2	9/19	40	Marked	Marked	Slight
2987	8/27	1⅓	8/28	30	Moderate	Moderate	Moderate to slight
3202	9/21	3	10/8	30	Moderate	Moderate	Moderate to slight
1496	7/4	11/12	7/5	30	Moderate	Slight Macewen anterior fontanel bulging	Macewen absent; fontanel slightly tense
3003	8/28	⅔	8/28	68	Very marked	Fontanel bulging; Macewen marked	Fontanel slightly depressed; Macewen absent
2801	8/18	3	8/18 8/20	40 40	Marked Marked	Moderate Marked	Moderate Moderate
3160*	9/15	1⅔	9/15	18	Slight increase	Marked	Marked

* Case 2710 shows a marked Macewen with all the accompanying evidences of hydrocephalus, yet on puncture only 15 c.c. of fluid were obtained under no pressure over the normal. A case of a somewhat similar character is No. 3160. In such instances it would certainly incline one to think that the edematous condition of the nervous tissue may become so marked, that the foramina of communication between the ventricles of the brain and the subarachnoid space of the cord may be partially and temporarily occluded, thus interfering with the usual circulation of cerebrospinal fluid.

Case 2790 showed a Macewen's sign which was doubtful; the spinal fluid was under normal pressure and no change was noted in the sign after puncture. Probably the sign would best have been called negative in the first place.

Cases 2858 and 2783 exhibited a slightly positive Macewen, 15 c.c. of fluid were removed under very slight pressure, flowing very slowly, little or no alteration in the sign was noted. This is what is usually encountered where the amount of fluid removed is so small as not to influence materially the relative position of cranial vault and its contents to one another.

Case 2797 showed no Macewen and yet the fluid was under moderate increased pressure and 28 c.c. were easily obtained. Probably here it was more a question of some physical changes in the bony envelope which interfered with proper conduction.

closely against the former and increasing the bone conduction so that a new note is produced on percussion.

It was not uncommon to see distinct evidence of pain exhibited on percussion of the skull. Thus, if the examination was carried on while a child was sleeping, he would frequently awaken and begin to cry; or in a stuperous case, the percussion would often arouse the patient to such an extent that he would show evident disapproval of its further use. In children old enough to talk, it was common to have them say that their head hurt and ask to be let alone. That this procedure should be painful during the early, acute period of the disease is not surprising when the severe degree of meningeal inflammation commonly present is considered.

While the subject of this paper has been purposely limited mostly to a consideration of Macewen's sign in poliomyelitis as utilized during the epidemic of 1916 at the Kingston Avenue Hospital, it would seem advisable to say that in subsequent studies we have found this sign equally as valuable in the detection and treatment of the hydrocephalus accompanying tuberculous and cerebrospinal meningitis and the various forms of meningism complicating the infectious diseases.

THE CURATIVE AND PROPHYLACTIC VALUE OF VACCINES IN PERTUSSIS *

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At present there is considerable difference of opinion as to the value of vaccines in the treatment of disease. It may be said, perhaps, that there is a tendency to grant them a less important position in therapeutics than was the case a few years ago. The use of vaccines in whooping cough, however, is still highly recommended by many who have had occasion to use this therapy in private and institutional practice. Recently Luttinger[1] reported favorably on the use of this vaccine after an experience with a whooping cough clinic in New York City. However, Van Sholle, Blum and Smith[2] concluded from the same clinical material that "more observations and more critical observations with controls for comparison must be made before the case can be made out for the curative and prophylactic value of pertussis vaccine." Their results were quite the opposite to those of Luttinger. Shaw[3] used pertussis vaccines as a prophylactic on 164 children exposed in four different epidemics, and found that only 7 per cent. of the number developed the disease.

It will thus be seen that there is a striking lack of uniformity in the conclusions. The present study is in a measure the continuation of one which was reported from this institution in 1914 by Hess.[4] In the course of an epidemic during that year various vaccines were used, including an autogenous strain, for the purpose of both curative and prophylactic therapy. This investigation was carried out on a large number of children, and the conclusion was drawn that although the vaccine did not seem to be of value in curing the disease or lessening its severity, it did seem to have some prophylactic value. Twenty of the children vaccinated, however, developed pertussis in spite of the prophylactic inoculations. In 1917, when this disease again visited our

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* Submitted for publication April 15, 1918.

*From the Home for Hebrew Infants, New York City.

[1] Luttinger, P.: Pertussis Vaccine, Jour. Am. Med. Assn., 1917, **68,** 1461.

[2] Van Scholle, A., Blum and Smith: The Therapeutic Value of Pertussis Vaccine in Whooping Cough. Jour. Am. Med. Assn., 1917, **68,** 1451.

[3] Shaw, H. L. K.: The Treatment of Whooping Cough. New York State Jour. Med., 1918, **18,** 18.

[4] Hess, A. F.: Use of a Series of Vaccines in the Prophylaxis and Treatment of an Epidemic of Pertussis. Jour. Am. Med. Assn., 1914, **63,** 1007.

institution, it was decided once more to attempt to determine the value of this therapy in pertussis. The cases may be divided into five groups:

1. Early prophylactic treatment.
2. Later prophylactic treatment.
3. Unvaccinated.
4. Curative vaccination.
5. Patients who had received prophylactic treatment in 1915 as well as curative or prophylactic treatment in this epidemic.

The vaccine used was that prepared by the municipal laboratory of New York City, and the dosage given was that which they recommend, and was in excess of that which had been used in the previous epidemic.

TABLE 1.—Data of Twelve Patients Who Developed Pertussis in Spite of Prophylactic Vaccination Two to Three Weeks Prior to Coming in Contact with Active Cases *

Name	Date of Vaccination	Date of Exposure	Date of Onset	Severity	Per Cent.	Duration (Weeks) of			Aver. Duration of Paroxysm, Weeks
						Cough	Whoop	Vomiting	
M. G.	7/6, 7/8, 7/10	7/22	9/29	Mild	..	4	1	0	
H. S.	7/6, 7/8, 7/10	7/22	8/24	Mild	..	6	6	0	
S. W.	6/28, 7/5, 7/11	7/22	8/15	Mild	..	8	6	0	
P. W	7/8, 7/10, 7/12	7/22	8/22	Mild	..	5	3	2	
M. H.	6/28, 7/5, 7/11	7/22	8/14	Mild	..	4	4	4	
S. B.	7/8, 7/10, 7/12	7/22	7/31	Mild	..	7	5	0	
A. B.	7/8, 7/10, 7/12	7/22	8/ 9	Mild	59	3	2	2	4
S. S.	6/28, 7/5, 7/11	7/22	8/31	Moderate	..	6	6	4	
I. J.	6/28, 7/5, 7/11	7/22	8/10	Moderate	16	6	5	2	5½
B. W	6/28, 7/5, 7/11	7/22	7/28	Severe	..	10	8	3	
M. K.	7/6, 7/8, 7/10	7/22	8/ 5	Severe	..	10	10	9	
A. G.	7/6, 7/8, 7/10	7/22	8/14	Severe	2.5	12	9	6	9

* Twenty-nine patients (70 per cent.) thus treated did not develop pertussis.

1. *Early Prophylaxis.*—In most prophylactic vaccination researches the question always has arisen as to whether the patients had not possibly become infected, and were not in the incubation period of the disease before the vaccine was resorted to. This is especially true in relation to pertussis, which has a long incubation period and indefinite onset. For example, if a child showed symptoms of the disease some ten days after vaccination, it could not be stated with certainty that the virus had not entered the body before the vaccines were resorted to We were particularly fortunate in this epidemic in being able to observe a group of patients to which this criticism was not applicable. It so

happened that forty-one children in the isolation house were given a series of vaccinations three weeks or more before they were transferred to the main building where the epidemic broke out. If we are to regard this period of time as sufficient for the child to produce its immune bodies, which would seem correct, judging from the analogy in animals, we can feel certain that these children must have been protected to the greatest possible extent. Table 1 illustrates the

TABLE 2.—Data of 114 Patients Who Developed Pertussis in Spite of Prophylactic Vaccination *

Length of Time Pertussis Followed Prophylactic Vaccination	Number of Cases	Severity	Average Duration (Weeks) of			Remarks
			Cough	Whoop	Vomiting	
2 weeks	27	Mild....... 9	4	2½	3 days	1 child had pertussis in 1914 also; received prophylactic vaccination in 1914
		Moderate. 4	8	6	3	1 child had prophylactic vaccination in 1915
		Severe..... 10	16	15	5	4 children received prophylactic vaccination in 1915
3 weeks	21	Mild....... 9	5	3½	4 days	1 child was exposed to whooping cough in 1915 and 2 had prophylactic vaccination in 1915
		Moderate. 5	9	6	3½	1 child received prophylactic vaccination in 1915
		Severe..... 7	11	7	6	
4 weeks	29	Mild....... 20	5	4	4 days	1 child received prophylactic vaccination in 1915
		Moderate. 5	7½	6	2	
		Severe..... 4	11½	10	4	3 children received prophylactic vaccination in 1915
5 to 7 weeks	21	Mild....... 12	5⅔	3⅔	2 days	
		Moderate 5	8	6	3	1 child received prophylactic vaccination in 1915
		Severe..... 4	11	11	3	2 children had a recrudescence after 5th week
8 to 12 weeks	16	Mild....... 9	3½	1	0	Very mild group of cases
		Moderate. 3	8	8	3 days	
		Severe..... 4	12	11	3½	1 case: recrudescence after 7th week

* One hundred and sixty-six children (59 per cent.) did not develop pertussis.

results on this group of cases. It will be seen that twelve developed pertussis, and that twenty-nine, or about 70 per cent., did not develop this disease. It will also be noted that although most of these cases were mild, there were three which were exceptionally severe, lasting on an average about nine weeks. We shall postpone drawing any conclusions from these results until we consider the next group of children who were also given prophylactic treatment.

2. *Later Prophylactic Treatment.* — This group consisted of 220 children who were in the building where the epidemic took place and were unavoidably exposed to infection, as there were active cases in each ward. They received prophylactic treatment in the same manner as the former group. Of this number, 114, or 41 per cent., contracted pertussis from two to twelve weeks after vaccination. About half of these cases were mild, especially those that came down from two to three months after vaccination, which may be due to the fact that the epidemic was already on the decline. The average duration of the paroxysmal stage will be noted to have been forty-two days (Table 2). It is of special interest that in this group, eleven children had prophylactic treatment during the 1915 epidemic of whooping cough and that nevertheless, in spite of this double protective therapy, they came down with the disease.

TABLE 3.—Data of Nine Unvaccinated Children Who Developed Pertussis *

Name	Severity	Duration (Weeks) of			Remarks
		Cough	Whoop	Vomiting	
G. I.	Mild	8	3	0	
H. F	Mild	7	4	0	
I. S.	Mild	4	2	0	
E. E.	Moderate	9	7	0	
H. C	Severe	16	12	7	Epistaxis; received prophylactic vaccination in 1915
H. C.	Severe	11	9	5	Received prophylactic vaccination in 1915
D. K.	Severe	11	6	3	Epistaxis
H. B.	Severe	18	16	8	
I. G.	Severe	15	14	7	Hematemesis

* Nine others did not develop this disease.

In view of the rarity of recurrence in pertussis we wish to report that one of our patients had whooping cough in 1914; this attack was very mild, lasting only twelve days.

3. *Unvaccinated.*—Of the eighteen children who did not receive any treatment, nine contracted pertussis. About one third followed a mild course; however, the average duration of paroxysmal coughing was about eight weeks.

TABLE 4.—Data of Twenty-Eight Patients Who Received Three Curative Injections

Name	When Treatment Began	Severity	Duration (Weeks) of			Remarks
			Cough	Whoop	Vomiting	
R. A.	6 days before onset	Mild	5	4	0	
L. B.	3 days before onset	Mild	6	5	0	Recrudescence after the 4th week
L. F.	8 days before onset	Mild	6	5	2	
S. S.	1st week after onset	Mild	3	2	0	
H. A.	1st week after onset	Mild	3	2	0	Received prophylactic vaccination in 1915
W. S.	1st week after onset	Mild	5	1	0	
G. C.	1st week after onset	Mild	5	1	0	
A. S.	2d week after onset	Mild	6	5	0	
H. S.	2d week after onset	Mild	6	4	3	
Ch. S.	3d week after onset	Mild	7	2	0	
H. S.	3d week after onset	**Mild, 39%**	7	1	0	
T. F.	6 days before onset	Moderate	7	4	1	
H. K.	8 days before onset	Moderate	9	6	0	
S. P.	1st week after onset	Moderate	8	3	2	
A. R.	1st week after onset	**Moderate, 14%**	7	5	2	Received prophylactic vaccination in 1915
I. W.	8 days after onset	Severe	16	13	5	Recrudescence after the 8th week
M. G.	8 days after onset	Severe	7	4	4	Hematemesis
G. C.	6 days before onset	Severe	21	21	7	Developed pneumonia and empyema; died
N. M.	4 days before onset	Severe	10	5	4	
A. K.	4 days before onset	Severe	9	5	1	
H. V.	8 days before onset	Severe	11	8	6	Received 4 injections
M. P.	1st week after onset	Severe	10	10	0	
S. K.	1st week after onset	Severe	15	13	12	Received prophylactic vaccination in 1915
H. S.	1st week after onset	Severe	11	8	4	Received 4 injections
M. L.	2d week after onset	Severe	8	6	6	
I. R.	2d week after onset	Severe	11	8	4	
M. G.	3d week after onset	Severe	24	24	20	Recrudescence after the 8th week
S. S.	8 days before onset	**Severe, 47%**	14	12	5	

4. *Curative vaccination.*—Twenty-eight children received the curative treatment by three injections of the vaccine. Some of the very severe cases received even four injections, the last two consisting of two billion bacteria.

TABLE 5.—DATA OF TWENTY-THREE PATIENTS WHO HAD RECEIVED PROPHYLACTIC VACCINATION IN 1915 AS WELL AS CURATIVE OR PROPHYLACTIC TREATMENT DURING THIS EPIDEMIC

Character of Vaccination	Number of Cases	Severity	When Treatment Began	Average Duration (Weeks) of			Remarks
				Cough	Whoop	Vomiting	
Curative	8	Mild, 4	First week	4	2	3 days	
		Severe, 4	First week	12	10	6	Two cases epistaxis
Prophylactic	15	Mild, 5	Two cases 2 wks. and three cases 4 wks. before onset	5½	3	1½	One case had whooping cough in 1914
		Moderate, 2	2 wks. after onset	7½	6	3½	
		Severe, 8	Five cases 2 wks. and three cases 4 wks before onset	12	11	5½	

TABLE 6.—SUMMARY OF TABLES 1, 2, 3, 4 AND 5

Group	No. of Cases	When Treatment Was Given	Number of Cases Contracting W. C.	Average Duration (Weeks) of			Per Cent. Not Developing W. C.	Severity of Disease, per Cent.
				Cough	Whoop	Vomiting		
Early prophylactic	41	6-12 wks. before onset	12	6	5	2	70	Mild, 59 Moderate, 16 Severe, 25
Later prophylactic	280	2-12 wks. before onset	114	8	6	2	59	Mild, 52 Moderate, 22 Severe, 26
Double prophylactic (1915 and 1917)	60	15 cases 2-4 wks. before onset, 8 cases 2-4 wks. after onset	23	7	6	3	61	Mild, 39 Moderate, 8 Severe, 53
Curative*	28	From 1 wk. before to 1-2 wks. after onset	..	9	5	3	..	Mild, 39 Moderate, 14 Severe, 47
Nonvaccinated	18	... .	9	9	8	3	50	Mild, 33 Moderate, 11 Severe, 56

* These cases received three injections

Naturally, we were able to begin treatment early; this is one of the advantages of a study of this kind, carried out in an institution with a physician in constant attendance. Indeed, we have included in this group of "curative cases" fifteen children who received injections three days to a week before manifesting symptoms of the disease. It will thus be seen that in our analysis we have given the therapy the benefit of every doubt. Table 4 gives the results in a conclusive manner. Without doubt the vaccine accomplished little, for 60 per cent. of the cases must be classed as severe.

In conclusion we would call attention to a group comprising twenty-three children who had received prophylactic treatment in 1915 as well as curative or prophylactic treatment during this epidemic, but who, notwithstanding this fact, contracted pertussis. We found that the duration and severity in these cases did not differ, to all appearances, from the other cases.

CONCLUSIONS

As a result of the use of vaccines in this epidemic of pertussis we are led to about the same conclusions which Hess reached in 1914 following a similar therapeutic test. It would seem almost certain that pertussis vaccine, given even in large dosage, not only has no curative effect, but does not tend to lessen the severity of the disease. The experiences of these two epidemics can be interpreted only in this way.

As regards the prophylactic value of pertussis vaccine, the case is different. In both the former epidemic and in this one the percentage of vaccinated children who developed the disease was considerably less than of those who were not vaccinated. If we draw conclusions from our own results we must therefore attribute to the vaccine some prophylactic potency.

We wish to emphasize the fact that in this study it was possible, for the first time, to vaccinate children some weeks before they came in contact with cases of pertussis, and that therefore there was no chance of their having been in the incubation stage at the time prophylactic therapy was instituted.

I desire to thank Drs. A. F. Hess and Sidney V. Haas for permission to publish this study, and Dr. Julius Blum, pathologist of this institution, for his assistance.

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FURTHER REPORT ON THE USE OF PERTUSSIS VACCINE CONTROLLED BY THE COMPLEMENT FIXATION TEST *

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In a previous communication[1] I gave a preliminary report on the prophylactic use of pertussis vaccine controlled by the complement fixation test. In this paper it was shown that, by means of the complement fixation test, it was possible to demonstrate specific antibody formation after the prophylactic injection of pertussis vaccine. The conclusions arrived at were as follows:

> Our observations in seventeen cases would, theoretically, justify the prophylactic vaccination against pertussis. In none of the cases treated with the smaller doses could any antibodies be demonstrated, whereas, large doses, such as recommended by the New York City Health Department, showed antibodies in 44 per cent. of cases. The freshly prepared vaccines were, apparently, more effective than the stock vaccines, as 60 per cent. of the patients treated gave positive fixation reaction. From this it may be concluded that it is possible to immunize children against pertussis if sufficiently large doses of freshly prepared pertussis vaccine be given.

Since that time it has been possible to continue and extend this work at the Minnesota State Hospital for Crippled Children.[2]

In the first series of four cases, a three months old vaccine, prepared by the New York City Department of Health, was used. Three doses of one-half billion, one billion and two billion bacteria were given on alternate days. The complement fixation test before the administration of the vaccine and two weeks after, was negative in all four cases. In the second series, of ten cases, a vaccine was employed, freshly prepared from three strains of Bordet-Gengou bacilli, in the same dosage of one-half billion, one billion and two billion bacteria, on alternate days. (Our original cultures were obtained through the courtesy of the New York City Health Department.) The complement fixation test, before the administration of the vaccine, was negative in all cases; two weeks after the last injection the test was markedly positive in nine cases and questionably positive in the tenth. A third series of four cases was given a com-

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* Read in the Section on Diseases of Children of the American Medical Association at its sixty-ninth annual session, Chicago, June 12, 1918.

* From the Department of Pediatrics and the Department of Bacteriology, University of Minnesota.

[1] Huenekens, E. J.: AM. JOUR. DIS. CHILD., 1917, **14,** 283.

[2] I wish to take this opportunity to thank Drs. Gillette and Christison for extending to me the privileges of the hospital.

mercial vaccine—from the label on the bottle, presumably two months old. This was given in three doses, one billion, one and one-half billion and two billion; all were negative before, two remained negative one week afterward, one was doubtfully and one definitely positive. Little significance was attached to a doubtfully positive reaction. A fourth series of nine cases gave a negative complement fixation test. A freshly prepared vaccine was then injected, every third day, in three doses of one billion, one and one-half billion and two billion. A complement fixation test performed one week after the last injection gave a markedly positive reaction in all nine cases. Of these last nine cases, three had slight temperature reaction after the second dose; none after the other doses. The fever was ephemeral, lasting but a few hours, in two cases reaching as high as 101 F.; in the third case 100 F. To summarize the last four series, four cases that were given three months old vaccine showed no evidence of antibody formation; four cases, given two months old commercial vaccine, gave a distinctively positive reaction in only one case, or 25 per cent. Of the nineteen given freshly prepared vaccine, eighteen gave a markedly positive reaction and one a questionably positive reaction, or 94 per cent. In the last nine cases, in which a larger dosage was used, one, one and one-half and two billion, there were 100 per cent. positive reactions and these could be elicited within one week after the last injection.

Studies were made to determine how long the positive complement fixation test persisted. Of the cases giving a positive reaction after the prophylactic injection of vaccine, it was possible to test thirteen after the lapse of three months. Three were found to be still positive; the other ten had become negative. With the lapse of six months, all reactions were negative, including the three who had still been positive at three months.

What is the significance of this? Does it mean that all immunity has been lost? Immunologists are agreed that, in such cases, while the antibodies may have disappeared from the blood, a considerable immunity still remains; for the patient, having once gone through the process of antibody formation, is able to repeat the process more readily and more quickly in subsequent infections. This is illustrated in typhoid fever, where the positive Widal reaction after a period of time disappears, but the immunity to typhoid persists.

It finally remained to be determined what constitutes a fresh vaccine. At what age does it begin to lose its efficacy? For this purpose three vaccines were prepared and were given, one when two weeks old, another when three weeks old and the third at four weeks. Twelve cases were employed, four for each vaccine, in the dosage of one, one and one-half and two billion. The four patients given four weeks old vaccine gave positive reaction in two cases, or 50 per cent., the cases given three weeks old vaccine gave 25 per cent. positive reactions, while the two weeks old gave 75 per cent. positive reactions. It follows, therefore, that a two weeks old vaccine has begun to deteriorate.

An interesting point in this connection is that the freshly prepared vaccine is very cloudy, while the older vaccines are clear or nearly so. Dr. Larson, of the Bacteriology Department of the University of Minnesota (to whom I am greatly indebted for assistance and helpful suggestions), has made the interesting observation, in his work with other vaccines, that autolysis sets in shortly after the preparation of a vaccine, that the process is usually complete in about three weeks, and that, as a result of this autolysis, the vaccine changes from cloudiness to a clear solution. He believes that an autolyzed vaccine has entirely lost its antigenic properties.

Another advantage of fresh vaccine is that no preservative is employed.

Pick[3] has shown that egg albumin which has been treated by some disinfectant, such as iodin, phenol or nitric acid, is materially altered, in that immune serum produced against such treated antigen does not react with normal antigen, that is, untreated egg albumin.

DISCUSSION

The fact that antibody formation takes place within a week after the third injection of vaccine would indicate that fresh pertussis vaccine may be used, not only as a prophylactic, but also in the treatment of the disease if the patient is seen in the early stages. This would mean that, owing to the difficulty of diagnosing pertussis in the early catarrhal stage, the vaccine should be employed on mere suspicion during an epidemic, especially where there is a history of known exposure. It may be argued that the difficulty in obtaining fresh pertussis vaccine is so great as seriously to interfere with its usefulness. But the difference in activity of freshly prepared and old pertussis vaccine is so marked, as proved conclusively by this work, that the attempt to put fresh pertussis vaccine on a practical basis should be made. Commercial laboratories, by constantly keeping on hand cultures of several strains of pertussis bacilli, should be able to supply the vaccine on short notice and at a moderate cost.

SUMMARY AND CONCLUSIONS

Pertussis vaccine from two to three months old, employed in very large doses, one billion and over, immunizes in only 12½ per cent. of cases.

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[3] Kolle-Wassermann: Handbuch, Vol. 1.

Two to four weeks old vaccine confers immunity in from 25 to 75 per cent. of cases.

Freshly prepared vaccine, employed in the same dosage, shows evidence of antibody formation in 94 per cent. of cases. When used in still larger doses, one, one and one-half and two billion, 100 per cent. positive reactions are obtained.

The antibodies are demonstrable within one week after the last injection.

The following conclusions, therefore, seem warranted:

Pertussis vaccine should be employed only when freshly prepared and without preservative. By fresh vaccine is meant a vaccine less than one week old.

The most effective dosage is one billion, one and one-half billion and two billion, given on alternate days, for three doses.

It is most effective as a prophylactic, but should be of great value in the early catarrhal stage of pertussis.

In doubtful cases of pertussis the vaccine should be administered before an exact diagnosis can be made, especially during an epidemic or where there is a history of previous exposure.

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A PROTECTIVE THERAPY FOR VARICELLA, AND A CONSIDERATION OF ITS PATHOGENESIS *

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As is well known, chickenpox is one of the very mildest of the infectious diseases to which children are subject. It possesses, however, considerable medical interest, as one of the group of diseases of unknown origin, and furthermore, because of its remarkable communicability. In the latter particular it is rivalled only by measles. In the Home for Hebrew Infants it has been our experience that in the course of an epidemic about three quarters of the younger children develop varicella, and about one half of those above 2 years of age. It spreads rapidly through the institution, progressing from ward to ward in an uncontrollable manner, frequently necessitating quarantine for a period of many months. Among children in private homes it possesses a serious pedagogic aspect, often disrupting the school sessions for long periods because of its widespread prevalence and long incubation period, which causes the infection to drag along throughout the entire winter term. Therefore, when Kling,[1] in 1913, reported that he was able to immunize children against this mild but exceedingly disturbing infectious disease by means of a single vaccination, we welcomed the announcement and decided to make use of it at the earliest opportunity. Kling's method consisted merely of applying the contents of the vesicles to the abraded surface of the skin, after the manner in which a von Pirquet tuberculin reaction is carried out. Two years later a small epidemic of chickenpox made its appearance in our institution and Kling's method was put into practice. The result may be summarized by the statement that it afforded a certain degree of immunity, but that it was by no means satisfactory. This, we believe, has been the experience of others who have used this procedure. It seemed to point the way, however, to better methods. It was evident, from its partial success, that the virus was contained in the vesicles, and it seemed probable that its failure was due to a faulty and uncertain introduction of the virus.

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* Read in abstract, May 6, 1918, before the American Society for Clinical Investigation, and presented before the American Pediatric Society, Lenox, Mass., May 29, 1918.

[1] Kling, C.: Berl. klin. Wchnschr., 1913, **50,** 2083.

During the past year varicella has been widespread throughout New York City, and made its appearance in our admitting pavilions. An opportunity was therefore afforded us again to attempt immunization. To this end we made use of the contents of the vesicles, but instead of applying this fluid to the surface of the skin, we injected it intravenously. The technic was as follows:

> In each instance only vesicles, and not pustules, were made use of; the surfaces were very gently washed with sterile salt solution and the contents allowed to ascend into capillary tubes. As much as possible of the clear fluid was obtained and was immediately mixed with sterile normal salt solution. This diluted virus was diluted still further with salt solution before it was injected. The dosage was entirely empirical, ¾ inch, as measured in the capillary tube, was used in each instance.[2]

In all, thirty-eight children, about 3 or 4 years of age, were vaccinated intravenously after this method. None of the children developed any local or general signs, or any eruption suggestive of varicella. They were all, in the course of the epidemic, unavoidably in contact with one or more cases of chickenpox, but in spite of this proximity only one developed the disease, this one thirty-six days after the date of inoculation.

It is evident, therefore, that by means of these intravenous vaccinations almost absolute immunity was brought about, and no symptoms of the disease. This result, paradoxical as it may at first appear, may be interpreted as follows: It would seem that most viruses are able to bring about their specific diseases only when they are introduced in their natural paths, or rather, that if they are introduced by other routes, an excessive amount of the virus is required to produce a specific reaction. Varicella, a disease of the lymphatic system, does not enter the body by means of the blood stream, and its virus has not acquired the property of invading the human organism by this path. It was this line of reasoning which led us to undertake this mode of therapy.

Camus[3] found, in his experiments on smallpox, that it required a very much larger amount of variola virus to produce this disease in rabbits when the intravenous, instead of the cutaneous, method was employed, and recently Noguchi[4] noted a similar phenomenon in experimenting with his testicular virus. The latter reports that in order to produce an eruption one thousand times more virus had to be introduced by way of the blood stream than applied on the skin.

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[2] All children in the institution who have a large spleen, bilateral epitrochlear glands, or give a family history of insanity, are subjected to the Wassermann test, so that all danger of syphilis was guarded against.

[3] Camus, L.: Compt. rend. Soc. de biol., 1913, **75,** 344.

[4] Noguchi, H.: Jour. Exper. Med., 1918, **27,** 425.

It is interesting to note in this connection that Noguchi showed that the lymph glands harbored the virus; this may likewise hold true for varicella.

The vesicular lymph was given also in other ways, as will be seen by consulting Table 1. It will be noted that in a number of cases it was introduced intravenously after having been inactivated by exposure to a temperature of 56 C. for three quarters of an hour. In sixteen instances the unheated lymph was injected intracutaneously; in ten, subcutaneously, and in a few cases was placed on the broken skin, on the mucous membrane of the nose, on the tonsils and buccal mucous membranes, and on the mucous membranes of the nose and mouth.

It seemed as if these methods might afford a simpler technic, and one which would avoid the somewhat difficult intravenous puncture. It will be seen from the table, however, that the number of these cases which came into intimate contact with the varicella were too few to allow us to judge of the success of these attempts at vaccination. Two facts, nevertheless, stand out in sharp relief: first, that no instance of primary varicella, even of the mildest type, resulted from these attempts at immunization and, second, that only the intravenous method was shown to afford adequate protection. The latter conclusion is inevitable in view of the fact that chickenpox developed about two months later in one of the three cases in which the lymph was placed on the broken skin (von Pirquet), and in two of the three cases in which it was applied to the nostrils. These few tests suffice to show the inefficacy of these simpler methods.

About three years ago Herman[5] made an attempt to immunize infants under 6 months by applying to the nostrils nasal mucus from children having measles. He carried this out in forty cases and believed that he had brought about immunity in a certain number of instances. In the light of this report, and its simplicity, it seemed worth while to make a similar attempt on a small number of cases in relation to varicella. In view of the fact that the vesicular lymph, which is known to contain the varicella virus, did not induce the slightest disorder when applied this way, it was evident that no disturbance was to be apprehended from this procedure. In three instances the nasal secretion of varicella patients was applied to the nostrils; in three others the tonsillar secretion to the tonsils, and in six, the tonsillar and pharyngeal secretions were transferred to the nose, the pharynx, and the tonsils. In none of these twelve cases was there any reaction whatever, either local or systemic. In two, secondary varicella developed in the course of the epidemic, from six to eight weeks later — one, where the nasal secretion was employed, and another where the tonsillar secretion was made use of. It is therefore evident that this method cannot be relied on to bring about protection. This is all the more striking in view of the fact that of these twelve cases only six came in intimate contact with varicella, so that we must consider that two of the six failed to develop immunity to the disease.

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[5] Herman, C.: Arch. Pediat., 1915, **32,** 503.

Incidentally, these tests furnish interesting information as to the portal of entry of the virus of varicella. The fact that the lymph from the vesicles, when applied to the broken skin or to the mucous membranes, led to no infection must cause us to consider this investigation from quite another standpoint. How are we to explain this lack of infectivity of the contents of the vesicles, which are generally regarded as the source of infection, and are used as the criterion in prescribing the duration of quarantine? There seems to be but one logical interpretation of these results, namely, that the lymph was in no instance applied to its natural portal of invasion. The only other possibility—that the virus is not present in the vesicle—is apparently refuted by our experience that immunity was brought about by injections of this fluid. What is, then, Nature's path of invasion? These vaccinations afford strong testimony — of a negative character, it is true — for an answer to this question. In view of our results, and the highly infectious nature of this disease, we are led to the tentative conclusion that the virus is air borne, and that its portal of entry frequently is the respiratory tract.

Summary of Protective Immunization

Mode of Introduction of Lymph	Number of Cases*	Number Subsequently in Contact with Chickenpox	Number of Contacts Developing Chickenpox	Remarks
Intravenous	38	38	1	Chickenpox appeared in this case 41 days following prophylactic therapy
Intravenous (inactivated)	9	1	0	
Intracutaneous	16	5	1	No local reaction
Subcutaneous	10	0	—	
Skin (v. Pirquet)	3	3	1	Chickenpox 62 days after immunization
Nostrils	3	3	2	Chickenpox 44 and 62 days after immunization
Tonsils and mouth	3	3	0	
Tonsils, nose and mouth	4	0	—	

* There was no instance of signs or symptoms of varicella occasioned by the immunization.

CONCLUSIONS

It is possible to bring about immunity to varicella by means of an intravenous injection of the contents of the vesicles. In thirty-eight instances in which this was carried out it failed to protect in only one case. Vaccinations of this kind induce neither local nor systemic reaction. The acquisition of immunity likewise indicates that the specific virus is contained in the vesicles. A simpler method of therapy, the application of the lymph to the broken skin or mucous membranes, failed to bring about satisfactory immunity, although it also occasioned no disorder.

These investigations have a secondary bearing as to the natural portal of entry of the varicella virus into the body. As we can exclude the skin and the mucous membranes in this connection, it would seem most probable that the virus enters by way of the respiratory tract, and that contagion comes about through the air. This mode of infection would account for the almost unexampled communicability of this disease.

16 West Eighty-Sixth Street.

ENERGY METABOLISM OF AN AMAUROTIC FAMILY IDIOT *

FRITZ B. TALBOT, M.D.
BOSTON

The following case of amaurotic family idiocy was obtained from the Children's Hospital through the kindness of Dr. John Lovett Morse, and studied under the direction of Dr. F. G. Benedict at the Nutrition Laboratory of the Carnegie Institution of Washington, Boston, Mass.

HISTORY OF CASE

History.—The child, B. D., girl, aged 2 years and 4 months, was admitted to the hospital Nov. 22, 1916. The father and mother, brother and sister were living and well, and were of normal mental and physical development. There was a normal family history.

The patient was born of a normal pregnancy and labor, and was breast fed for one year, during most of which time she had a severe facial eczema. At 3 to 4 months she first noticed her hands, but never made any effort to use them except to play with a rattle, when it was placed in them. If she dropped the rattle, she was unable to find it, nor could she pick it up if her hands came in contact with it by accident. She never played with anything else, and had never been able to hold up her head or sit up.

Dec. 24, 1915, she had a convulsion during which the extremities jerked for an hour or more, the eyes were rolled up, and she perspired and drooled. In February, 1916, she entered the Infants' Hospital and Dr. George H. Derby found on examination of the eye grounds, "secondary atrophy of the optic nerve heads, and cherry-red spots in the macular regions with edema about them." She entered the Children's Hospital because she was mentally backward, could not see, and was only able to take liquid food. She took no notice of her surroundings, and lay quietly except when startled by a noise, which could cause a temporary clonic convulsion of all the extremities. Except during these periods of spasm, she lay absolutely still, without any voluntary movement.

Physical Examination. — This showed an underdeveloped, poorly-nourished child, lying quietly in bed, drooling constantly and taking no notice of the surroundings. The extremities were cold and the feet slightly blue. The head was large in proportion to the body. Both pupils reacted to light, but the right was slightly larger than the left. They were regular in outline. The physical examination otherwise revealed nothing abnormal except that the extremities were spastic and markedly atrophied. There were no signs of voluntary motion. The von Pirquet test was negative. The white count was 9,800. The urine was acid, cloudy, straw colored and contained the slightest possible trace of albumin. The sediment contained many pus cells. Lumbar puncture, 8 c.c., clear fluid under normal pressure. Cell count 7, of which one was a leukocyte and six were epithelial cells. The Wassermann reaction was

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* Submitted for publication June 4, 1918.

* Read at the meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

* From the Nutrition Laboratory of the Carnegie Institution of Washington, Boston.

negative. From December 5 to 12, the week preceding the time that the metabolism was observed, the child's temperature was subnormal, the lowest being 95.5 F. At times during this period the pulse registered 69. This was lower than the careful pulse records taken during the metabolism periods. She never cried and lay absolutely quiet in bed except when disturbed by a sudden, loud noise or by being touched. External stimuli of this sort caused clonic convulsive movements. During this period she simply existed in bed, taking her food as it was given to her. She died Dec. 26, 1916, probably of inanition as a result of pyelitis and amaurotic family idiocy.

Necropsy.—Postmortem examination by Dr. S. B. Marlow showed a few facts of importance when taken in connection with the metabolism. The body was 75 cm. long and showed extreme emaciation. The skin was everywhere loose, and even on incision showed no subcutaneous fat. The muscles were atrophied and showed very little rigor mortis; they were pale and thin in appearance. There was no fat in the mesentery or the retroperitoneum. In fact, the absence of fat was so conspicuous that special emphasis was laid on it in the report of the pathologist. The brain nowhere filled the cranium and was from 0.5 to 1 cm. distant from the bony wall of the skull. The dura over it was loose and collapsed, giving the impression that it had been previously distended with fluid. The meninges about the spinal cord were edematous and distended. The eye when removed showed at the macula a deep colored spot about 1.5 cm. in diameter, surrounded by a gray ring 2 mm. wide. The rest of the examination showed nothing of importance to record here.

The child had, therefore, amaurotic family idiocy and pyelitis. She was extremely thin and emaciated, and moved in bed only when disturbed by sound or touch. The amount of muscular activity during the day was so slight that it was almost negligible, except during the colonic convulsions. There was no storehouse of fat on which to draw for energy when desired, as is found in the new-born infant. Although most of the remaining body tissue was muscle, bone and organs, the muscles were thin and atrophic, and could not, therefore, be said to represent normal muscle. Although clinically the actions of this infant were similar to those of the child without any cerebral hemispheres, previously reported by me,[1] physically the two infants were quite different. In this case there was an almost complete absence of fat, while in the other, the body was composed almost entirely of fat. Table 1 gives the energy metabolism of B. D. The length of the periods of observation of this baby and the babies subsequently reported was, in all instances, thirty minutes.

Although the weight of these normal infants is quite close to, and in most instances almost identical with, that of B. D., their length is much shorter and, therefore, they are much fatter. However, they give an idea of what B. D.'s metabolism should have been if the body had been developed normally in relation to the weight. The basal metabolism of B. D., compared to that of three normal infants of the same weight, is very low (approximately 30 per cent. lower than the normal for the weight).

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[1] Talbot, F. B.: Arch. Pediat., 1915, **32,** 452.

TABLE 1.—Basal Energy Metabolism of B. D.*

Date	Body Weight and Surface	Height, Cm.	Heat Produced per 24 Hours				Average Pulse Rate	Relative Activity
			Total Cals.	Per Kilogram, Cals.	Per Sq. Meter			
					Lissauer, Cals.	DuBois Linear, Cals.		
12/11/16	6.41 kg. $10.3\sqrt{wt_2} =$ 0.355 sq. m. Du Bois Linear = 0.408 sq. m.	76	283†	..	...	...	83	Active
			246	38	693	603	83	Quiet
			250	39	704	613‡	86	Quiet
			250	29	704	613	91	Quiet

* One ounce of milk was taken four hours before observations were commenced.

† Preliminary period not used in calculation.

‡ Average respiratory quotient, 0.82. Temperature, rectal, 97 F. beginning of periods: 96.8 F. at end of periods.

TABLE 2.—Comparison of Basal Metabolism of B. D. with That of Normal Infants of Approximately the Same Weight

Name	Age, Mos.	Body Weight Without Clothing, Kg.	Height, Cm.	Heat Produced per 24 Hours				Periods Averaged	Pulse Rate
				Total Cals.	Per Kilogram, Cals.	Per Sq. Meter			
						Lissauer, Cals.	DuBois Linear, Cals.		
1. B. D.	28	6.41	76	249	39	700	610	3	87
2. M. C.* (normal infant)...	4	6.17	63	333	54	967	...	7	103
3. R. A.* (normal infant)...	7	6.42	65	358	56	1,002	...	3	118
4. N. D.* (normal infant)...	7	6.79	67	381	56	1,032	...	5	100

* Benedict and Talbot: Am. Jour. Dis. Child., 1914, 8,, 1.

TABLE 3.—Comparison of Basal Metabolism of B. D. with That of Normal Infants of the Same Age

Name	Age, Mos.	Body Weight Without Clothing, Kg.	Height, Cm.	Heat Produced per 24 Hours				Periods Averaged	Pulse Rate
				Total Cals.	Per Kilogram, Cals.	Per Sq. Meter			
						Lissauer, Cals.	DuBois Linear, Cals.		
1. B. D.	28	6.41	76	249	39	700	610	3	87
2. M. R.*........	25	10.96	79	617	56	1,214	1,135	3	104
3. Gr. Mc.L.*.....	26¼	12.24	88	605	49	1,107	1,028	3	96
	29½	12.82	91	602	49	1,101	1,025	4	112

* Not previously reported.

The metabolism of these normal infants gives an idea of what the metabolism of B. D. would have been had she developed normally for her age. Her total metabolism is less than half that of three average normal infants, and her metabolism per unit of body weight or body surface were both decidedly low.

The metabolism of this amaurotic family idiot is, therefore, very low both when compared to that of normal infants of either the same weight or normal infants of the same age. Her metabolism is comparable to that of J.J. M. who had no cerebral hemispheres,[1] and, therefore, moved only when stimulated to do so by touch. This child moved both when touched and when disturbed by noise. The body was run at such a low economic level that very little food was necessary for life.[1]

TABLE 4.—Comparison of Metabolism of Pathologic Children

Name	Age, Mos.	Body Weight Without Clothing, Kg.	Height, Cm.	Heat Produced per 24 Hours				Pulse Rate
				Total Cals.	Per Kilogram, Cals.	Per Sq. Meter		
						Lissauer, Cals.	DuBois Linear, Cals.	
1. B. D.	28	6.41	76	249	39	700	610	87
2. J. J. M.	8	8.43	73.5	239	28	560	...	73
3. Cretin, C. G.[2]	44	11.83	85	464	39	867	...	95

The interpretation of the metabolism of B. D. is extremely difficult, as we have a picture of great emaciation, in which a large proportion of the body tissues are muscle with almost no fat. The pulse rate, which, at the time of the observation, was relatively high or normal for the age,[3] was low at times in the hospital. Under these conditions a high metabolism rather than a low metabolism might have been expected, as has been recorded in the findings of Publication 201 of the Carnegie Institution of Washington. As a matter of fact, the metabolism was very low. The rectal temperature of 97 F. during the period of observation was not an extremely subnormal temperature, but it is not impossible that this may be an indication of lowered vital activity, although it is quite unreconcilable with the relatively high pulse rate.

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[2] Talbot, F. B.: Am. Jour. Dis. Child., 1916, **12**, 145.

[3] In designating the pulse rate of B. D.—83 to 91, as shown in Table 1—as high, or relatively high, it must be remembered that it is not logical to say the pulse rate in a given individual is abnormally high. It has been often pointed out in the Nutrition Laboratory of the Carnegie Institution of Washington, that it is not permissible to argue that a high pulse rate in any given individual absolutely implies a high metabolism. What is more important is the deviation from the normal pulse rate of that individual.

In conclusion, this child with amaurotic family idiocy presents a very unusual and complicating situation, in which the metabolism may have been modified either by the subnormal temperature, by emaciation, by the plane on which the baby was living, or by the disease, and does not present any simple explanation. It is hoped that other records of the metabolism of amaurotic family idiots will clear up the doubtful point presented in this picture.

311 Beacon Street.

A COMBINED TEMPERATURE, WEIGHT, FOOD, SYMPTOM, ETC., RECORD CHART FOR PEDIATRIC WORK *

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The putting down on one sheet in a graphic and easily legible form the most important factors concerned in determining the picture and the course of a disease, as well as the therapy instituted to control it, is obviously a great advantage over the old and still quite universally practiced method of using different sheets for different data. The newer method not only saves much time, but enables one to correlate at a glance many of the observations into a picture of the whole. The idea is not original, as it was seen and used by one of us in its developed form in 1910 at the Kaiserin Augusta Victoria Haus in Charlottenburg.

The chart of this institution was ruled for thirty-one days, and was a most elaborate affair, providing not only for recording the temperature, pulse, respiration, weight, food, stools, symptoms, treatment, calories, etc., but also for various data regarding the parents, the confinement, the diagnosis and condition on admission and discharge, etc. In consequence it was awkwardly large, measuring approximately 15¼ by 20½ inches, and in addition the proportion of the length to the width of that part of the chart recording the weight made the angle of the weight curve too acute, about 23 degrees for a daily gain of 30 gm., which, according to Heubner, as quoted by Langstein and Meyer,[1] should be 39° 45′ for an average daily gain of 26.6 gm. during the first three postnatal months. These dimensions also made impossible much of a rise or fall in the weight chart, except as a result of a very large gain or loss, 20 gm. gain or loss causing a movement of the curve for a vertical distance of but 7/48 of an inch. Finally, the temperature, pulse and respiration charts could hardly be ruled accurately with an economic use of time, as no vertical rulings existed in the chart, except the lines separating one day from the other. On the whole, however, this chart was an improvement, and it was with the idea of applying its good points to our local hospital records that the present chart was devised.

As it was our idea to have all of the pediatric wards in which local medical school teaching was being carried out use the same chart-

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* From the Babies' Dispensary and Hospital, City Hospital and Lakeside Hospital, Cleveland.

* Read by title at the meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

[1] Langstein and Meyer: Säuglingsernährung und Säuglingsstoffwechsel, J. F. Bergmann, 1910, p. 41.

ing and recording scheme, in order to aid in making the whole department uniform, we were bound closely to the present forms and sizes of the records of Lakeside Hospital and City Hospital, the Babies' Dispensary having adopted for its Out-Door Ward no rigid form or size of chart. Consequently, the largest electrotype that we could use was one measuring 8⅝ inches in width and 10⅝ inches in length, which at Lakeside Hospital had to be printed on paper measuring 8⅝ by 11 inches, while at City Hospital and at the Out-Door Ward of the Babies' Dispensary and Hospital the more spacious sheet of 9½ by 12 inches could be used. Our present ideas regarding a more ideal size will be indicated further on.

In the chart here presented the following innovations or changes have been made:

1. The space for the recording of the weight and food has been given dimensions which make possible the formation of a weight angle of about 35 degrees with a daily gain in weight of about 30 gm.

2. As a result of this change there has been made available more space for the recording of "Treatment" and "Symptoms." In this connection it may be said that the symptoms are not described in detail, but simply given in an appellative manner. Whenever a detailed description is desirable, this must be noted in the regular history sheet.

3. The space for the individual day has been divided by three vertical lines into four spaces. This arrangement makes it possible for the nurse quickly and easily to find the correct space for the notation of the temperature degree and pulse and respiration rates, according to the hour of the day. By dividing the daily space into four parts, it is possible to make an accurate notation of the pulse, respiration, etc., every twelve hours, every six hours, or every three hours. While the space for the last is small, yet experience has shown that it is ample, owing to the ever-present oscillation in the different curves.

4. The second of the third vertical lines mentioned under 3 has again been divided into ten equal parts, so that it really is an equally divided dotted line. This has been done to give the recording nurse an accurate and rapid guide for the notation of the temperature degree, the weight figure and the pulse and respiration rates. The last two are not frequently recorded, however, so the division is usable mainly in the registering of the temperature curve and the weight curve. Although the weight curve occasionally goes down into the food space, the dotted line has not been extended down beyond the space for the registering of the temperature curve, in order sharply to differentiate the one large space from the other.

5. The space for the recording of stools has been divided into the two periods, a. m. and p. m., and it has also been increased in size, in order that the individual stools might be described if desired.

6. The electrotype has been printed in a light coffee-brown or a light gray, in order that the colors used in recording the temperature, pulse, weight, and respiration might stand out more clearly. Von Pirquet has also used a different color than black for his charts, but the one he chose, a brownish-yellow, is difficult to see with artificial light.

At the Kaiserin Augusta Victoria Haus, a color scheme was used for the charting of the different food mixtures. In one department of that institution different colored and gummed paper slips were properly pasted into the food space, while in the other department the different colors were put on the food chart by using crayons. The former scheme is possibly somewhat neater, but also more complicated, as the various food modifications require a definite color of their own. With the crayon method fewer colors are necessary, because two colors can be used together in a corresponding proportion to designate the corresponding quantity of the foods as they exist in the food mixture, and if a nurse is at all careful and sketches the colors with a light hand, a very neat and permanent record can be made with simple and inexpensive crayons that can be purchased in the market.

On the pediatric service at Lakeside Hospital the chart and the following definite color and figure scheme have been used exclusively for fifteen months consecutively, so that a practical test really has been obtained.[2] Only a few minor changes in recording the feedings have been made.

Food Chart.—The colors named have been used to designate the following foods:

Whole milk, ultramarine blue
Skimmed milk, prussian blue
Whey, cobalt blue
S. M. A., violet
Plain buttermilk, chrome green, light
Koeppe's buttermilk, olive green
Casein milk, green, medium
Water, magenta
Oatmeal water, English vermilion
Barley water, madder lake
Potato water, Indian red
Cornstarch water, venetian red
Keller's soup, burnt umber
Keller's soup, modified, gold ochre
Tea, yellow
Breast milk, orange
"Refused," black

The total amount of food taken is sketched into the proper space of the food chart. If the amount taken does not correspond to the amount ordered, the difference is sketched in black above the amount taken, so that the space filled in with black designates the amount refused, and the total space occupied by both black and the food color represents the total amount ordered. As a result of this innovation of charting the amount refused in the manner described, one obtains a beautiful picture of the appetite of the child.

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[2] Much credit and appreciation in this connection are due Miss L. O. Essery and Miss M. Francis, head nurses of Wards A and K, Lakeside Hospital.

If it is desirable to note the amount of water taken by the child besides the food, this is either noted in one of the free spaces below the "Additional Nourishment" space or (and this is the plan which we have adopted) it is charted in the daily "Food" space, in the color corresponding to water, just as the food is charted in the same space, except that the amount of water taken is charted from the top down and the food from the bottom up.

The actual mixtures in the daily food are indicated in direct proportion in the color scheme. So, if an infant is to have one-third milk and two thirds oatmeal water, one-third of the daily food space up to the figure representing the amount taken is colored with ultramarine blue, and two-thirds with English vermilion.

The percentage and kind of carbohydrate or salts (sodium chlorid, sodium bicarbonate) added to plain water or to the different food mixtures are indicated by writing with a hard black crayon, in the upper part of the food color column, the following letters and figures:

L = Lactose
S = sucrose
D = dextrose
Lv = levulose
DM = dextri-maltose
M = Mellin's food
MS = malt soup

SC = sodium chlorid
SB = sodium bicarbonate
1 = 1 per cent. of total mixture
1½ = 1.5 per cent. of total mixture
2 = 2 per cent. of total mixture
2½ = 2.5 per cent. of total mixture
3 = 3 per cent. of total mixture, etc.

So the appearance of "3 S" just below the top of a 600 c.c. color column, representing one-third milk and two-thirds oatmeal water, would indicate that 18 gm. of sucrose had been added to the total to make a 3 per cent. addition of sucrose to the 600 c.c. mixture of one-third milk and two-thirds oatmeal water.

The number of feedings in twenty-four hours is noted just above the bottom of the color column for a given food mixture by writing in black with a crayon, Roman figures corresponding to the number of feedings ordered. In the foregoing example a "VI" in black at the bottom of the 600 c.c. column — one-third milk and two-thirds oatmeal water—would mean that the child was to receive 6 × 100 c.c. in twenty-four hours.

If a change in the food should be ordered, and so during one day a child receive two kinds of foods, the first mixture given is sketched at the bottom of the column and the second directly above it.

Illustrative examples of most of the points just made can be found in the accompanying charts.

Additional Nourishment Notes.—The additional nourishment column is used for the recording of vegetables, cereals, zwieback, etc.

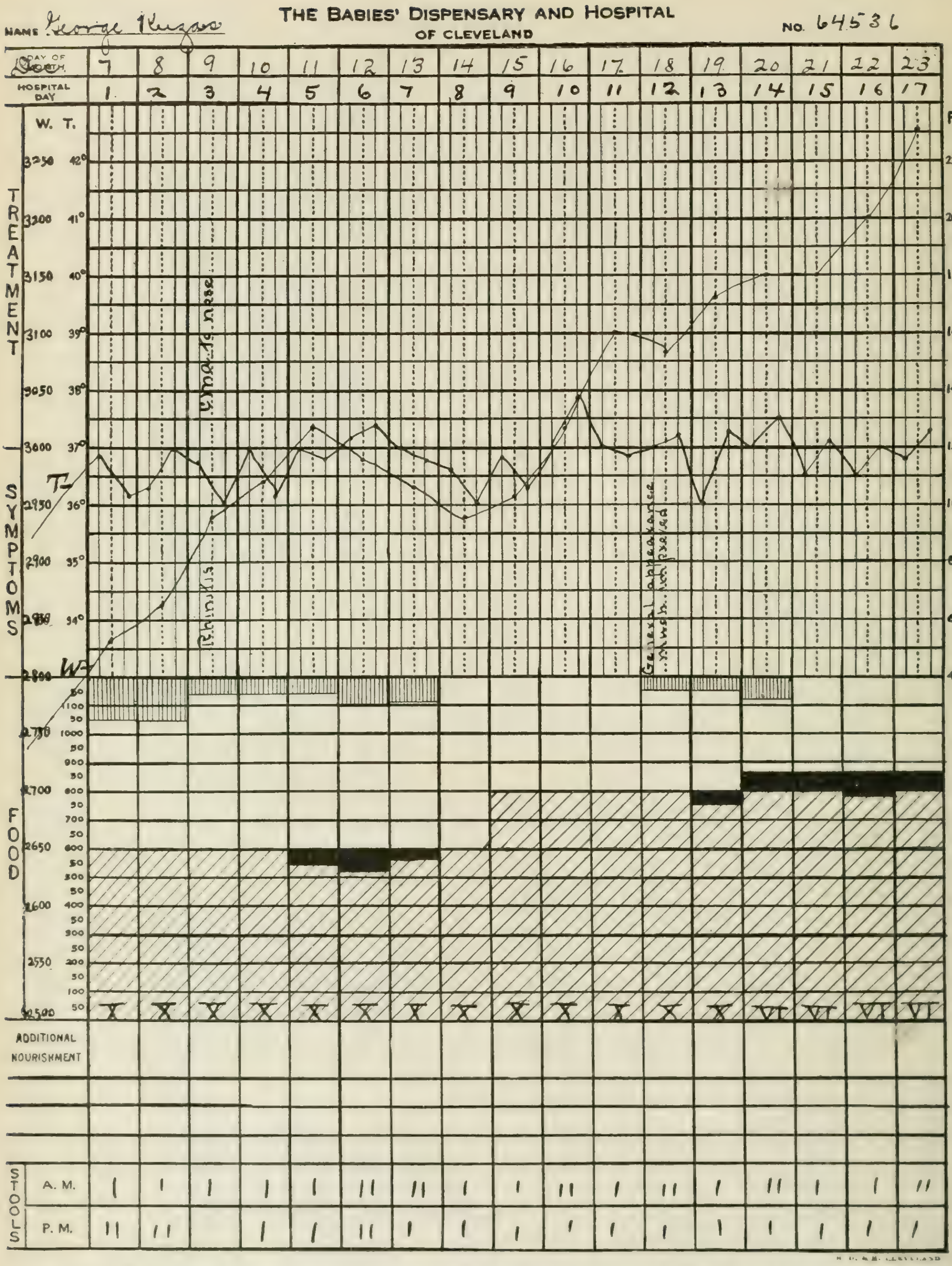

Fig. 1.—Example of authors' chart in use. The black line marked "T" is the temperature curve; the line marked "W" in the original chart is in red ink and is the weight curve. The portion shaded with diagonal lines represents Synthetic Milk Adapted and in the original chart in practical use is colored violet. The portion shaded with vertical lines represents water and in the chart in practical use is colored magenta. A complete description of the color scheme and other data recorded on the charts will be found in the text. About two-thirds actual size.

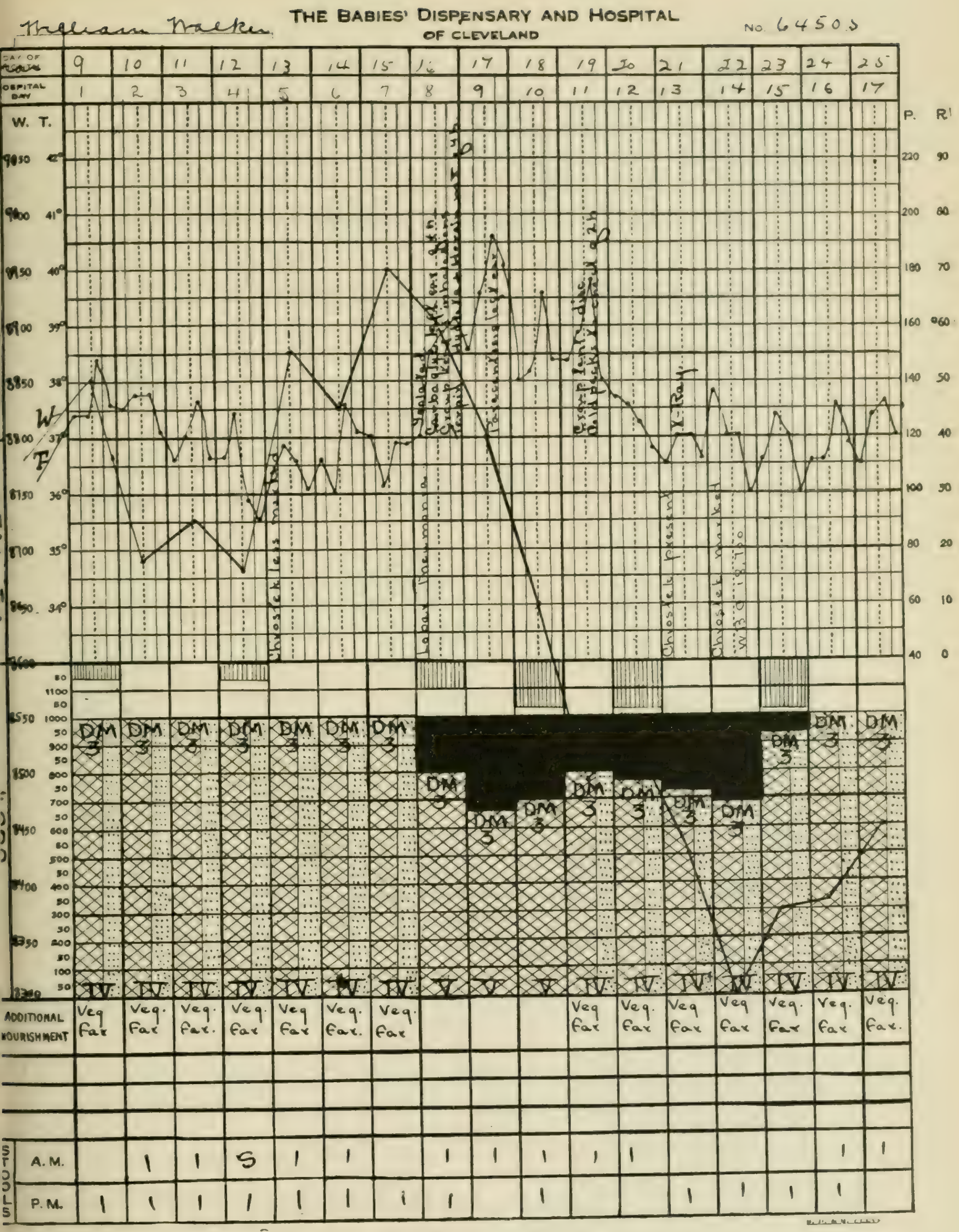

Fig. 2.—Another example of authors' chart. The lines T and W indicate temperature and weight urves, respectively. The lattice hatching represents whole milk and in the chart in practical use this rea is colored ultramarine blue; the dotted columns represent oatmeal water and in the chart as used n the hospital the area is colored English vermilion; the portion shaded by vertical lines represents vater and in the chart in use is colored magenta. About two-thirds actual size.

Weight, Temperature, Pulse and Respiration Chart.—The weight curve is sketched in red ink (W); the temperature curve in black ink (T); the pulse curve in purple ink; and the respiration curve in green ink.

Symptoms and Treatment Notes.—The treatment notes are written in red ink on the chart by the nurse, and the symptoms in black ink by the intern or clinical clerk. Two colors are used clearly to separate these contiguous notes, and the black has been used for the recording of the symptoms simply because it is desired to make these notations during the ward visit or immediately after, and, under these circumstances, black ink is at all times available, in the form of the ordinary black ink fountain pen, for every intern and clinical clerk.

Stool Chart.—The color scheme has also been utilized, together with the sign scheme, in the recording of stools.

The following crayon colors are used to indicate the following stool colors:

Crayon	*Stool*
Chrome yellow, medium	Lemon yellow
Gold ochre	Yellow-brown
Orange	Orange-carrot yellow
Madder lake	Beet red
Chrome green, light	Yellow-green
Chrome green, dark	Green
Olive green	Gray-slate
Burnt umber	Brown—Keller's, older children, hemorrhage
Black	Bismuth—old blood

| = formed soft stool.

\ = semi-solid, soft stool of salve-like consistency.

╲ = a thin stool whose consistency is between a watery stool and a semi-solid, salve-like stool. In many children this is not abnormal.

— = watery stool and abnormal, as far as consistency is concerned.

〰 = squirting, watery stool seen only in marked diarrhea.

′ = mucus, slight in amount.

″ = mucus, medium in amount.

‴ = mucus, marked in amount.

c = choppy, stringy stool, usually greenish-yellow and with mucus = dyspeptic stool.

C = casein curds.

s = soft, putty-like, or partly sandy, semi-solid, gray, yellowish-gray, or greenish-gray fatty soap stool.

S = hard, dry, pale gray, very light yellow or green-gray fatty soap stool.

F = soft, thin, shiny fatty stool, usually yellowish.

b = blood streaked on outside of stool, usually bright red and mechanical in origin.

B = blood, mixed well with stool and usually with pus, of a brown-red tomato-sauce color, seen mainly in enteritis follicularis.

H = blood, bright red or dark brown or black, when very large in amount, and due to hemorrhage, as in intussusception, typhoid or hemorrhagic diseases.

P = pus, usually mixed with blood, in enteritis follicularis.

Metric System.—It will be noticed that only the metric system has been used in this chart. This is in conformity with the plan which one of us inaugurated at the Babies' Dispensary during 1906, since which time all of the weight amounts, temperature degrees, and food amounts have been determined according to the metric system, not only for the physicians and nurses, but for the public as well, and it has been continued for added reasons: (1) in practically all scientific work of the various civilized countries the metric system is used, and (2) we believe that if it is more generally used in practical institutions like hospitals, dispensaries, etc., it will help toward its adoption by the public at large for their own daily personal use.

Pasting of Chart Sheets.—Even with the smallest sheet, $8\frac{5}{8}$ by 11, it is possible, if so desired, to make one continuous chart out of the individual seventeen-day chart sheets by simply using a photographic trimming knife and library paste.

Ideal Chart Size.—Earlier in the article it was indicated that the form of the chart as presented today was determined by local conditions, and that ideally we should prefer a somewhat different form. From the experience which one of us has had at Lakeside Hospital during a period of fifteen months, this ideal electrotype size should at present measure $9\frac{23}{24}$ inches wide by $13\frac{14}{15}$ inches long. The increase in width would add three days to the chart, making a total of twenty days. The increase in length of the present chart is applied as follows:

1. The "Temperature" space is increased to $6\frac{3}{4}$ inches.
2. The "Food" space is increased to $4\frac{1}{20}$ inches.

These alterations will change the angle of the weight curve for a daily gain of 25 gm. to 37° 21′, which would correspond with Heubner's figures of 39° 45′ for an average daily gain of 26.6 gm. This change also gives still more space in the "Symptom" and "Treatment" columns for the respective notations.

3. The "Additional Nourishment" space is increased to $\frac{35}{48}$ of an inch.
4. The blank spaces for extra notes under the "Additional Nourishment" space are increased in number from three to four.

This new form could be printed on paper measuring 10 by $14\frac{3}{8}$ inches, corresponding with $8\frac{5}{8}$ by 11 in the present chart, or better on a larger sheet measuring $10\frac{7}{8}$ by $15\frac{3}{8}$ inches, corresponding with $9\frac{1}{2}$ by 12 in the present chart.

IS THE AMOUNT OF CALCIUM USUALLY GIVEN IN DILUTIONS OF COW'S MILK INJURIOUS TO INFANTS?*

A REPLY TO THE ARTICLE ON "CALCIUM IN ITS RELATION TO THE ABSORPTION OF FATTY ACIDS," BY BOSWORTH, BOWDITCH AND GIBLIN, IN THE AMERICAN JOURNAL OF DISEASES OF CHILDREN, JUNE, 1918

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NEW YORK

The claim is made by Bosworth, Bowditch and Giblin that by the use of a special "reconstructed" or "decalcified" milk, infants who are artificially fed will have a no greater excretion of fat in the feces than those fed at the breast. The position is taken that this special milk provides an improved form of feeding over simple cow's milk dilutions, because on the latter, children suffer a serious loss of fat through the excretion of soap stools; also that there follows from such feeding excessive constipation, leading frequently to a general upset, termed by the authors a "blowup."

We have had no opportunity to study Bosworth's decalcified milk and its effects; but we desire to present some conclusions drawn from results obtained in this laboratory which may perhaps allay the fears of calcium injury from the use of simple dilutions of cow's milk in infant feeding.

There are three questions suggested by this article which we desire to discuss:

1. Is there a serious loss of fat (otherwise than through diarrhea) when the usual simple dilutions of cow's milk are fed?

Of a group of thirty-two children from 2 to 15 months of age whom we have studied, eight received over 25 gm. of fat daily, the highest intake being 47 gm. None of the entire group had any tendency to diarrhea. Twenty-nine had a fat retention of 89 per cent. or more of the intake, eighteen having over 90, and ten over 95 per cent. Only two of the whole group retained less than 80 per cent. of the intake, these retaining 78.9 and 78.2, respectively.

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* From the Laboratories of the Babies' Hospital and the Rockefeller Institute for Medical Research, New York.

Table 3 in the article by Bosworth, Bowditch and Giblin, when analyzed, shows much lower percentages of fat retained than the foregoing values. Of the twenty-three cases in their table, only ten show a fat retention above 84 per cent., only two over 90 per cent. and none over 95 per cent., while in eleven the fat retention is less than 80 per cent. The difference between their results and ours is brought out in Table 1.

TABLE 1.—Comparison of Figures for Fat Retention

	Bosworth et al.	Babies' Hospital Laboratory
Per cent. of total number with over 95 per cent. retention	0.0	31.3
Over 90 per cent	8.7	56.3
Over 84 per cent	43.5	90.6
Under 80 per cent	47.8	6.2

We have not found such low percentages of fat retained as their figures show, except in cases of diarrhea, and occasionally in infants fed on protein milk. In the latter the intake of fat and the absolute retention are usually higher than with other milk preparations.*

The extremely low fat retentions shown in Table 3 of the article by Bosworth, Bowditch and Giblin raises the question whether in all their cases the excretion reported fairly corresponds to twenty-four hours' intake, or is excessively large because of a diminished excretion on the preceding day or two. This possibility occurs to us because of the peculiarity of the calcium excretion given in their Table 1. Computing from the formula used — fat 2 per cent., sugar 6 per cent., protein 1.6 per cent. — and the daily intake of 795 c.c., the total calcium intake could not have been more than 0.70 gm. of calcium oxid (CaO). The total calcium excretion reported is 1.697 gm., an excess over the intake of nearly 1.0 gm. of CaO. This we consider to be most improbable, being greater than we have ever found, even in the most severe cases of rickets. Such excretion, however, might be accounted for, if the stools had been small, or if there had been none on the two preceding days. On this supposition the intake for three days would be approximately 2.1 gm., making, with the excretion reported, a positive balance of 0.4 gm., or about 0.13 gm. per day, which is a small retention. The daily fat excretion would then become about 1.84 gm., giving a retention of 14.06 gm., or 88.5 per cent. of the intake, a not unusually low retention for perfectly normal infants.

Bosworth and Bowditch claim that the high calcium content of the intake causes a serious loss of fat as soaps in the stools of bottle-fed infants. Accordingly, we present below some figures which may tend to reassure those who are likely to be alarmed over the "abnormality" of the large quantities of calcium soaps in the stools. In the group of thirty-two children just referred to, nineteen were receiving calcium to the extent of over a gram of CaO daily. Of these, only six had as much as 2 gm. of fat as soaps in the daily stools. All but one were utilizing over 85 per cent. of the ingested fat, while four absorbed more than 95 per cent. Table 2 shows the per cent. of fat retained and the amount of fat excreted as soaps by the children in this group who had the highest calcium intakes.

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* The protein milk employed in the Babies' Hospital is made from whole milk, not from skimmed milk.

TABLE 2.—Fat Retention and Fat Excreted with High Calcium Intake

Gm. CaO Intake	Per Cent. Fat Retained	Gm. Fat Excreted as Soap
1.80	95.8	0.78
1.66	89.4	1.68
1.50	93.2	1.12
1.47	87.7	0.79
1.41	87.1	1.76
1.39	95.5	0.99

A study of Table 2 shows that the maximum output, in the feces, of calcium bound as soaps was about 0.18 gm., since the combining weight of the higher fatty acids found in the stools is about ten times that of calcium oxid. Thus, it can be seen that the calcium which goes to form soaps is only a small part of the calcium intake.

Bosworth and Bowditch claim, however, that it is the degree of solubility of the calcium of the food which influences the formation of soaps. Using Bosworth's estimate of the "condition of calcium in cow's milk," which he gives in Table 6, the soluble calcium is seen to form 29.2 per cent. of the total calcium. In our entire series of thirty-two cases previously mentioned, the calcium which could possibly be held as soaps invariably falls below 25 per cent. of the intake. In the six with very high intake of calcium, the amount of calcium which could be held as soaps ranges from 7.0 to 12.5 per cent. of the intake, running well below half of Bosworth's estimate of the soluble calcium of the food. This proves conclusively that not all the soluble calcium is eliminated in the feces in the form of soaps. The inference that a high calcium intake causes a serious loss of fat does not seem to be warranted.

In a group of forty-six breast-fed infants, whose stools have been studied in this laboratory, twenty-five had over 40 per cent. of the fat excretion in the form of soaps. Thus, the presence of a considerable proportion of calcium soaps in the stools cannot be called an "abnormality," if breast-fed infants are to be taken as a standard. In one case, in which an exact record of the intake of breast milk was obtainable, the following results were found. With an intake of 41.9 gm. of fat, the total fat excretion was 2.26 gm., of which 63.8 per cent. was soap. The fat retention was 94.6 per cent. of the intake. The calcium intake was 0.355 gm. This child was at the time doing extremely well and has continued to do so. In this baby with a small calcium intake, practically the same results were found as with many bottle-fed infants with two or three times the calcium intake. This child had for its age (about 1 month) an unusually large fat intake.

It is conceded that breast-fed infants retain a high *percentage* of their fat intake and in many cases retain a large actual *amount* of fat. This may possibly be due to the biologic factors of the natural food rather than to any advantage in its chemical composition. Bosworth and Bowditch maintain that the soap excretion is dependent on the proportion of soluble calcium in the food, and on this ground explain the lower soap fat excretion when the food is breast milk. According to their Table 6, however, cow's milk, after being diluted with an equal volume of water, contains but little more soluble calcium than does breast milk, that is, 0.0225 gm. of calcium in 100 c.c., in comparison with 0.021 in breast milk.

2. Is there danger of constipation with serious consequences in infants fed on simple dilutions of cow's milk?

Among the stools from the thirty-two children before mentioned, there was only one which from its appearance could be called constipated. The child was 7½ months old and was doing well with an intake of 47.0 gm. of fat daily. The retention was 93.7 per cent. of the intake, the excretion of soap fat 2.3 gm. daily. The child has continued to gain and has done well without interruption up to the present. Two other children, 14 weeks and 8 months of age, respectively, were reported to be constipated. Though the stools of the latter were induced by a daily enema, the feces of both these children were soft and pasty and the daily amount small. They had, respectively, a retention of 96 and 97 per cent. of the intake, with daily soap fat excretion of 0.5 and 0.3 gm. This sort of constipation depends rather on the muscular tone of the bowel and on training than on the chemical composition of the stool. A tendency to constipation in infants receiving simple cow's milk dilutions is generally controlled without great difficulty. On the other hand, the desirability of formed or semiformed soap stools in contrast to the ever dreaded tendency to diarrhea in bottle-fed infants, particularly in evidence in hospital patients, can hardly be overestimated. It is probably for this reason that protein milk with its high calcium and fat content plays so important a part in the control of diarrhea. Necessarily the formed stool has a large proportion of its fat in the form of calcium soaps, but, as has been previously emphasized, the total loss of fat in this way is very seldom, if ever, of serious consequence.

3. May there not be a danger in too low a calcium intake?

Unless the harm caused by a fairly high calcium intake can be quite definitely demonstrated, it would seem safer to allow an excess of calcium in the intake rather than to run any risk of providing less calcium than is needed for the normal growth of the bones. A number of cases of so-called intestinal infantilism have come under our observation. The most significant fact in the history of these cases is the extremely low intake of calcium in their previous feeding. The large calcium requirement of children with a tendency to rickets hardly needs mentioning in this connection. The calcium in breast milk, though smaller in quantity, may be more available than that of cow's milk; however, it is well known that many cases of rickets and tetany occur in children fed too long exclusively on breast milk.

In conclusion, we believe it is yet to be demonstrated that infants fed on simple dilutions of cow's milk do not retain an adequate amount of fat, when the stools are formed or semiformed and soapy; nor do we think that a high calcium intake necessarily causes a large fat loss in the feces; while a great reduction of the calcium in the food of infants may be attended with considerable risk.

PROGRESS IN PEDIATRICS

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NEUROBLASTOMA SYMPATHICUM

REPORT OF A CASE, WITH NOTES ON TWO OTHERS, AND A BRIEF REVIEW OF THE LITERATURE *

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BOSTON

Case 1.—Charles C., 4 years and 3 months old, was admitted to the Children's Hospital, Dec. 31, 1917. His family history was good. He was born at full term, and had always been well, except for rather frequent "colds" during his infancy. His mother thought that his abdomen had always been large, but she had not noticed it especially until two weeks before, since when it had increased in size very rapidly. He began to fail rapidly about the same time and the last week had been confined to bed. Since being in bed he had been somewhat short of breath and had had an unproductive cough. His appetite was fair, he did not vomit and his bowels were regular. He had no symptoms pointing to trouble in the urinary tract.

Physical Examination.—He was pale and poorly developed, and showed some evidences of old rickets. His tongue was slightly coated. The throat, heart and lungs were normal. The abdomen was markedly distended and the superficial veins slightly enlarged. The lower border of the liver was palpable, hard and sharp, 6 cm. below the costal border in the right nipple line, 8 cm. below the ensiform and running under the left costal border in the anterior axillary line. The surface was smooth, hard and slightly tender. The spleen was not made out. The kidneys were not palpable and there was no unusual resistance in the flanks. There were no evidences of free fluid in the abdomen. The genitals were normal and the rectal examination was negative. There was slight edema of the legs. There were no evidences of any involvement of the nervous system.

The urine was acid and cloudy from urates, but contained no albumin or sugar. The sediment was negative.

The blood showed: hemoglobin, 60 per cent. (Sahli); red corpuscles, 2,000,000; white corpuscles, 5,500; mononuclears, 40 per cent.; transitionals, 4 per cent., and polynuclear neutrophils, 56 per cent.

The red corpuscles showed slight achromia, but no variation in size or shape.

The tuberculin test was negative to both the human and bovine types.

The Wassermann test was negative.

The liver increased very rapidly in size, and edema of the scrotum, back and legs became marked. He lost very rapidly in weight and strength and died Jan. 6, 1918, one week after his admission and three weeks after the symptoms were first noted.

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* Submitted for publication June 3, 1918.

* From the Children's Hospital.

* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

The diagnosis during life was sarcoma of the liver, which, in spite of the rarity of the condition, was thought to be primary rather than secondary, because no primary focus of disease could be found elsewhere.

Necropsy.—A restricted necropsy was performed by Dr. S. B. Wolbach, fifteen and a half hours after death. The head was not opened. The throat, heart, lungs, gastro-intestinal tract, pancreas and pelvic organs showed nothing abnormal. The peritoneal surfaces were smooth and glistening. The mesenteric lymph nodes were not enlarged.

Liver: The lower border of the liver extended down to the crest of the right ilium and in the median line was 14 cm. from the ensiform. The enlargement of the liver was almost symmetrical. The suspensory ligament was pushed over to the left owing to the great enlargement of the right half of the liver and the anterior border of the right lobe was deeply notched a few centimeters to the right of the median line of the body. The liver weighed 2,050 gm. The capsule was smooth. The color was pale red and reddish yellow, mottled with fatty, opaque areas which were not elevated above the surface. These areas varied in size from 1 mm. to 1 cm. in diameter. The liver was extremely friable. Section showed surfaces bearing very little resemblance to normal liver tissue (Fig. 1). As a whole, the cut surfaces had a translucent appearance. There were distinct areas of translucent white tissue, circular in shape, all produced by the confluence of circular areas, thickly distributed throughout the whole of the liver. There were other large areas 4 to 15 mm. in diameter which were soft, deep red and bulging slightly from the cut surfaces. Here and there were narrow bands and small areas of brownish liver tissue, but everywhere paler than normal. It was quite evident that the whole of the liver was infiltrated with a soft new growth.

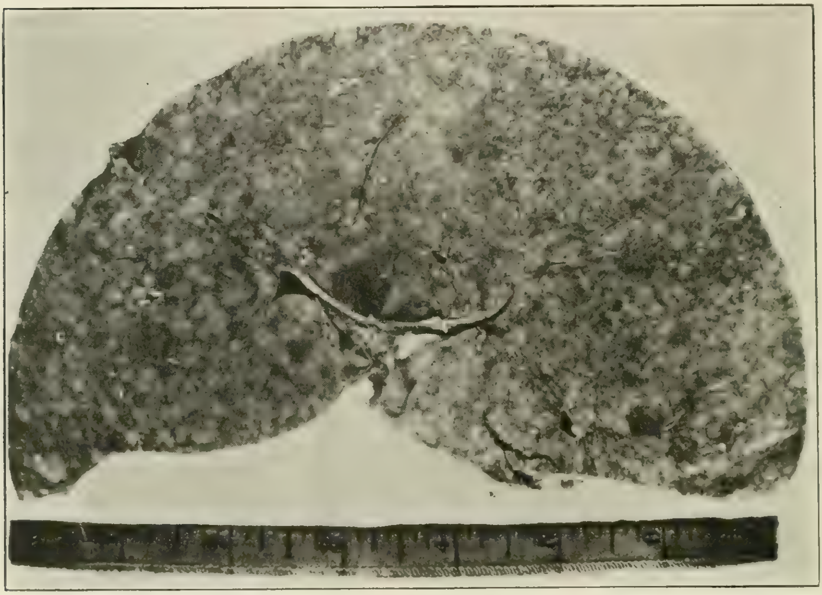


Fig. 1.—Photograph of a section of a Kaiserling specimen of the liver, Case 1. The scale is in inches.

The gallbladder and bile passages were patent and normal. Accompanying the cystic duct was a lymph node, 8 by 4 mm., which was soft, translucent white.

Spleen: The spleen was enlarged and measured 10 by 6 cm. The capsule was smooth; the color, salmon red. On section the cut surfaces were everywhere smooth and normal in appearance, except for a slightly paler color than is normal. The splenic corpuscles were visible and appeared normal.

Kidneys and Adrenal Glands: The kidneys were normal in size, color, markings and consistency. Partly overlying the left kidney and extending to the median line was a tumor mass (Fig. 2). The kidney itself was not connected with this tumor growth. Section of the tumor mass revealed its intimate relation with the adrenal gland. The tumor mass, as a whole, including the adrenal gland, was 8 cm. in length and 4 to 5 cm. in width. The superior end of the adrenal gland was recognizable. There was a triangular piece of adrenal present which measured 2.5 by 2.5 cm. Extending downward behind the tumor mass was a band of adrenal cortex, 4 cm. in length and from 6 to 8 mm. in width. This arm of the adrenal was not adherent to the tumor mass as a whole. In the center of the triangular portion of the adrenal gland first mentioned, was an elevated, white tumor nodule 8 mm. in diameter. Beneath this there bulged from the substance of the adrenal a tumor mass, 5 cm. in length, composed of three nodules, the superior one, 1 cm. in diameter, the middle one 3 cm., the inferior 2 cm. A section through the adrenal showed that the first mentioned tumor nodule extended into the substance of the adrenal and a cut section showed irregular borders. The color was grayish white. Beneath that there was a nodule, 1 cm. in diameter, soft and dark red. Section of the largest nodule, which was 3 cm. in length, presented in part firm white friable tissue, in part dark red necrotic material with many small gritty areas. The inferior nodule composing the main tumor mass was dark red, soft, and apparently composed of necrotic tumor tissue. There were numerous large lymph nodes lying between this tumor mass and the median line and grouped around the celiac exis. These lymph nodes varied in size

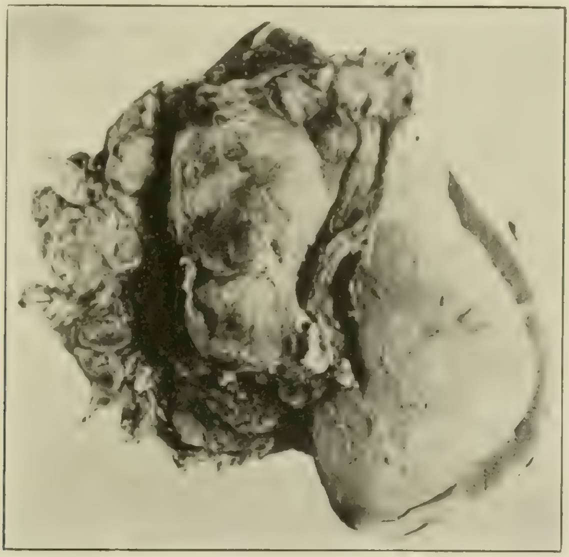


Fig. 2.—Photograph of the primary tumor of the adrenal and the kidney, Case 1.

from 3 to 8 mm. On section they were soft, translucent and white. The right adrenal gland was normal.

Frozen Section of Tumor: Frozen sections of the tumor, after hardening in formaldehyd solution, showed in the liver almost complete replacement of the liver parenchyma by small round cells with deeply stained nuclei. In some places the destruction of the liver tissue was complete, in others the liver columns could be recognized much flattened and distorted.

Sections of the tumor of the adrenal showed a small round cell tumor with a delicate reticular framework. Portions of this tumor were necrotic and portions were fibrous, but other portions showed a rosette grouping of the cells surrounding a central granular or fibrillar mass, characteristic of ganglioma embryonale sympathicum or neuroblastoma sympathicum.

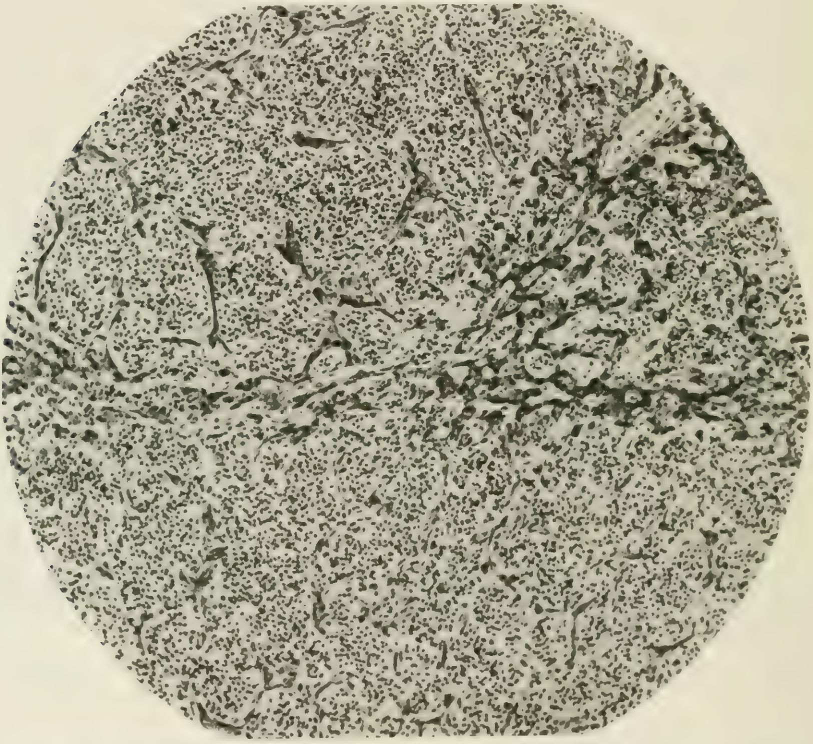
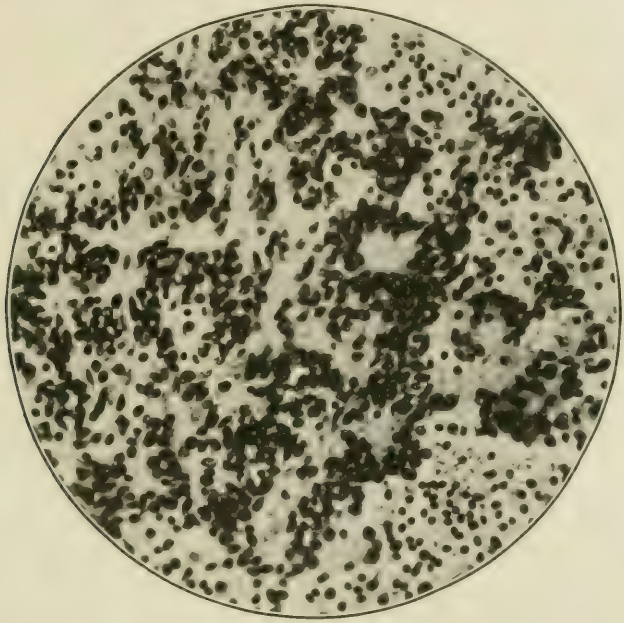


Fig. 3.—Low power photomicrograph of a section of the liver, Case 1; about 125 diameters.

Microscopic Examination.—The tissues were fixed in Zeuber's fluid and stained with eosin-methylene blue.

Liver: There is very little liver tissue remaining. The organ was largely replaced by a new growth consisting of exceedingly minute cells, smaller than lymphoid cells, most of them with densely staining homogeneous nuclei, having the appearance of pyknotic or postmortem nuclei. This appearance of the nuclei is probably due to richness in chromatin, as the preservation of other cells, that is, liver cells and bile ducts, is perfect (Fig. 3). The liver tissue is present in the form of anastomosing strands, in which the liver cells are usually much distorted, but occasionally they are almost normal in appearance. The intervening tissue filled with the tumor is traversed with delicate epithelial tubules, which probably represent regenerated bile ducts. In other places, where the tumor is actively invading, there are all degrees of atrophy and degeneration of the liver cells, and it is possible to see that the tumor cells are growing between the liver columns and endothelium of the sinusoids, although in most places such details of structure are entirely obliterated. The tumor cells are small, the cytoplasm is extremely scanty in amount and difficult to demonstrate. There are occasional clusters of slightly larger cells with nuclei less densely stained and containing scattered particles of chromatin. The cells, however, are embedded in a finely granular material, which in places can be seen to have a linear striated effect suggestive of protoplasmic fibrils. In some portions of the liver the replacement by tumor cells is so complete as to obliterate all trace of liver. There are many mitotic figures among the tumor cells.



4. Photomicrograph of the primary tumor of the adrenal gland, Case 1; about 400 diameters.

Adrenal Gland: Sections through the adrenal gland containing the primary tumor showed the bulk of the tissue to be composed of minute cells similar to those in the liver metastasis. There are places, however, where there is a very perfect "rosette" formation, consisting of larger cylindrical and pyriform cells arranged about a central mass of granular material (Fig. 4). This central granular material can be resolved in places into very delicate fibrils and the latter in some instances can be traced into the pyriform tumor cells. The stroma consists of a delicate vascular fibrous tissue. The tumor is a rapidly growing neuroblastoma, of sympathetic ganglion cell origin.

Lymph Node: Sections of a lymph node adjacent to the tumor mass showed complete replacement by the exceedingly minute type of tumor cells.

Celiac Ganglia: These are almost completely replaced by the tumor cells, which are always of the very small type.

Spleen: The malpighian bodies are of normal size and shape. A few contain hyaline masses and reticular hyaline material. The pulp contains many eosinophils of the myeloid type. The venules contain groups of cells which are possibly tumor cells, since many of them were smaller than lymphocytes and have deeply stained nuclei.

Kidneys and Right Adrenal Gland: These were normal.

DISCUSSION

From the liver alone the diagnosis of neuroblastoma would have been impossible to prove, although warrantable, as numerous instances are recalled in which the cells in the metastases from neuroblastomata primary in the adrenals have had the appearances characteristic of this case. The diagnosis in this case is established by the presence of the tumor in the adrenal showing a greater degree of differentiation of the cells evidenced by the formation of protoplasmic fibrils and the arrangement into ball masses which in section produce the rosette appearance.

The essential element in the tumor for diagnosis is the fibrils. The fibrils are not to be compared with the coarser, more or less specifically staining fibrils associated with connective tissue and neurogalia cells. They are in reality delicate protoplasmic processes and are representative of axis cylinder processes. There is no special stain for their demonstration.

The earliest diagnosis based on the presence of these fibrils in malignant tumors of the adrenal gland was that of glioma. Virchow[1] and Marchand[2], in 1891, recognized the nervous character of a tumor of the adrenal and compared the cells with the neuroblasts of the fetal sympathetic ganglia.

J. H. Wright[3], in 1910, focused attention to this group of tumors and collected twelve cases, including four of his own. He briefly and succinctly showed that the tumor cells associated with the fibrils have the "same morphology as the cells from which the sympathetic nervous system and the medulla of the adrenal develop and which are regarded by embryologists as arising from migrated primitive nerve cells." Wright offered the names neurocystoma and neuroblastoma as equally applicable.

Pick and Bielschowsky[4], in 1911, in a classification of tumors of nerve tissue origin, gave the name ganglioma embryonale sympathicum to the tumors described by Wright. Pick[5], in 1912, collected a total

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1. Virchow: Die Krankhaften Geschwulste, Berlin, 1863-1865.
2. Marchand: Festschr. f. R. Virchow; Internat. Beitr. z. wissensch. Med., Berlin, 1891, 578.
3. Wright, J. H.: Jour. Exper. Med., **12,** 556.
4. Pick and Bielschowsky: Ztschr. f. d. ges. Neurol. u. Psychiat., **6,** 391.
5. Pick: Berl. klin Wchnschr., **49,** 16.

of eighteen cases, including one of his own, and discussed fully and adequately the origin and the relationship of the tumors arising from the primitive nerve cells. These tumors may represent any of the potentialities of the primitive cells, which are nerve cells, glia cells and chromaffin cells. The tumors representing nerve cells with which we are now dealing may be either rapidly growing and undifferentiated or more slowly growing and more highly differentiated into ganglion cells. He completely substantiated Wright's conclusions.

Landau,[6] independently of Pick, in the same year, published a similar classification and discussion of these tumors. He added three cases of his own and uses the name malignant sympathetic neuroblastoma. From this time on the origin and classification of these tumors has been accepted and numerous new cases have been added.

The paper of Herxheimer,[7] in 1913, covers substantially the same ground as those of Pick and Landau. He chooses Landau's name, neuroblastoma sympathicum, in preference to Pick's ganglioma embryonale sympathicum, a choice which has proved to be in accordance with the preference of subsequent writers.

Two American papers, each introducing a new case, by Wahl[8] and Lehman,[9] are comprehensive and adequate to orient any one desiring more information on the subject of neuroblastoma. Lehman has collected a total of twenty-five cases of sympathetic neuroblastomas and several doubtful cases.

Hertz and Sacher's[10] case is the most recent one recorded and in the rapid growth of the liver metastasis bears some resemblance to our case.

Our case is noteworthy for the rapidity of the growth of the liver metastases, which overshadowed all other signs, and the absence of apparent metastases elsewhere. As a complete necropsy was not permitted, early metastases to the bones can not be excluded. It is our opinion that these tumors are not as rare as the small number of published cases would indicate and for this reason we append the reports of two other cases from the surgical service of the Boston Children's Hospital.

CASE 2.—W. D. MacN., aged 7 months, was admitted June 12, 1917. His past history and family history are irrelevant. May 4 a physician noticed a mass in the right side of the abdomen which was not tender and which did not noticeably increase in size. The physical examination showed a well nourished infant. The skin, eyes, ears, nose, mouth and throat were all negative. The heart and lungs were normal. The reflexes were normal. The abdomen showed a bulging in the right upper quadrant. Palpation showed a hard irregularly shaped mass occupying the whole of the upper and a third of the lower right quadrant. It was not tender. It descended with respiration, was not attached to the abdominal wall and by rectal examination the lower end was found to be freely movable.

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[6] Landau: Frankfurter Ztschr. f. Path., **11,** 26.

[7] Herxheimer: Beitr. z. path. Anat. u. Path., **57,** 112.

[8] Wahl: Jour. Med. Research, **30,** 205.

[9] Lehman: Jour. Med. Research, **36,** 309.

[10] Hertz and Secher: Hospitalstidende, **60,** No. 45; abst. Jour. Am. Med. Assn., 1918, **70,** 278.

An exploratory operation was done on June 14. The tumor was found to be inoperable and a small piece was removed for microscopic examination. The abdomen contained a slight excess of fluid in the flanks. The tumor was hard, nodular and not cystic and extended from the right costovertebral angle to below the brim of the pelvis and inward beyond the median line. It overlay the aorta and vena cava. The ascending colon was displaced forward and inward and crossed vertically the median aspect of the tumor.

Death occurred seven hours after the operation. Permission for a necropsy was refused.

The material was fixed in Zenker's fluid and stained with eosin-methylene blue, Mallory's phosphotungstic acid hematoxylin, Van Gieson's stain and hematoxylin and eosin. The photomicrographs were made from sections stained with hematoxylin and eosin.

Microscopic Examination.—The tumor is composed mainly of small round cells irregularly arranged in masses which are separated by a delicate fibrous tissue stroma giving an alveolar appearance. The tumor cells vary in size and the nuclei contain a variable but large amount of chromatin. The cytoplasm is small in amount and usually difficult to demonstrate. There are groups of larger elongated cells in compact masses but there is no rosette grouping in the sections. Delicate fibrils are very numerous throughout the tumor between individual cells and in large masses of parallelly arranged wavy fibrils lying between the groups of tumor cells and stroma or extending between adjacent clumps of tumor cells. There are many mitotic figures and a rare type of larger cell with abundant cytoplasm suggesting a ganglion cell. The tumor is a typical malignant neuroblastoma sympathicum identical with many of the reported cases (Figs. 5 and 6).

Case 3.—Myrtle P., aged 2 years and 2 months, was admitted to the outpatient department, March 2, 1918, for swelling and tenderness at the left knee, attributed to a fall one week previously. The knee was swollen, not red, slightly tender. There was limitation of motion to 20 degrees extension and 60 degrees flexion. A roentgenogram made March 5 shows widening of the lower end of the diaphysis of the femur with areas of rarefication just above the epiphyseal line. A mass was noticed in the abdomen and the child was admitted to the hospital March 9.

Her past history and family history are irrelevant. The child was well nourished and well developed. The cranium, eyes, ears, nose, teeth, mouth and throat were negative. The heart and lungs were normal. The reflexes and skin were normal. The extremities with the exception of the left knee were normal. The abdomen was rounded and tympanitic, with the exception of the left upper and middle quadrants. In the left upper quadrant there was felt a hard rounded mass which did not move when the position of the child was shifted. It was smooth, not tender.

An operation, March 11, showed a large tumor of the left kidney. This was enucleated and found to be adherent posteriorly. It extended upward to the diaphragm, where there was a cyst. The cyst ruptured and a considerable quantity of brown semisolid material escaped. After removal of the tumor there was but little bleeding from the cavity, but inspection showed that there were nodules of the growth extending downward along the vertebral column and out into the broad ligament on the left side.

Death occurred March 28, presumably hastened by a low grade infection of the peritoneum.

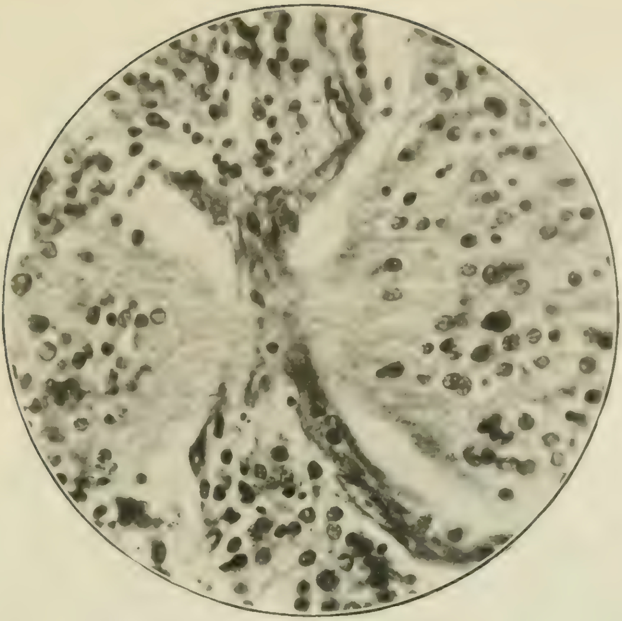

Figure 5

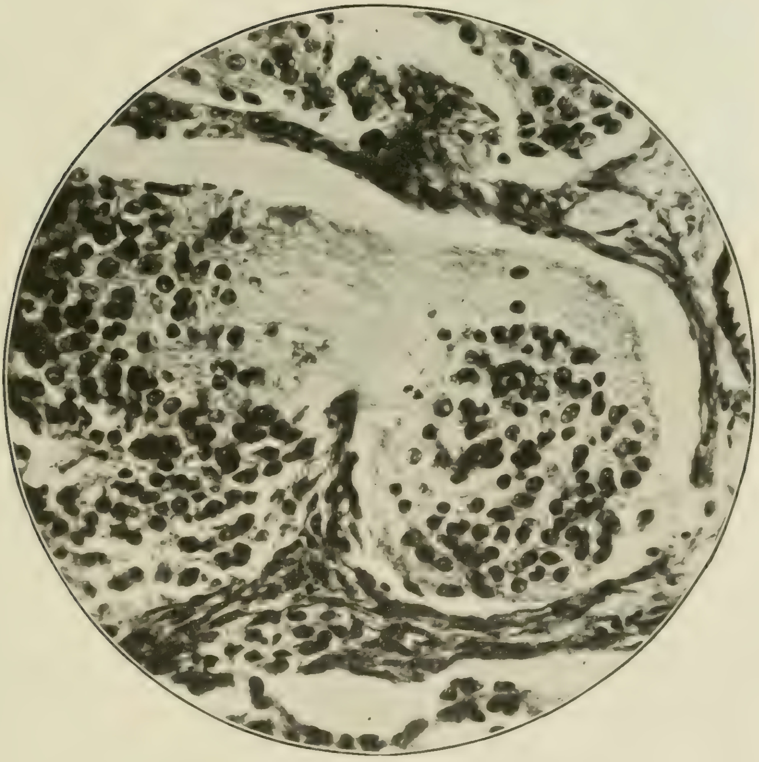

Figure 6

Figs. 5 and 6.—Photomicrographs from Case 2, showing masses of fibrils extending between clumps of tumor cells; about 400 diameters.

Pathologic Report.—The specimen consisted of a kidney partly replaced by tumor. It was moderately firm and measured 13 by 7 by 5 cm. The lower pole was evenly rounded. At the upper pole there was a loss of substance involving the pelvic border of the kidney, about 3.5 cm. in diameter. There was in this location an irregularly circular yellow and red mottled crater, the base of which was formed of granular friable material. At the periphery of this crater there was attached a grayish membrane continuous with the capsule of the kidney and which probably was the remains of the capsule overlying the necrotic mass. A section through this pole of the kidney showed an irregular zone of yellowish red mottled tissue, 1 to 2 cm. deep, and inferior to this the kidney substance appeared to be normal.

Microscopic Examination.—The tissue was fixed in Zenker's fluid and 10 per cent. formaldehyd. The description is based on sections stained with eosin-methylene blue, Van Gieson's stain and Mallory's phosphotungstic acid hematoxylin stain. The photomicrographs were made from sections stained with hematoxylin and eosin.

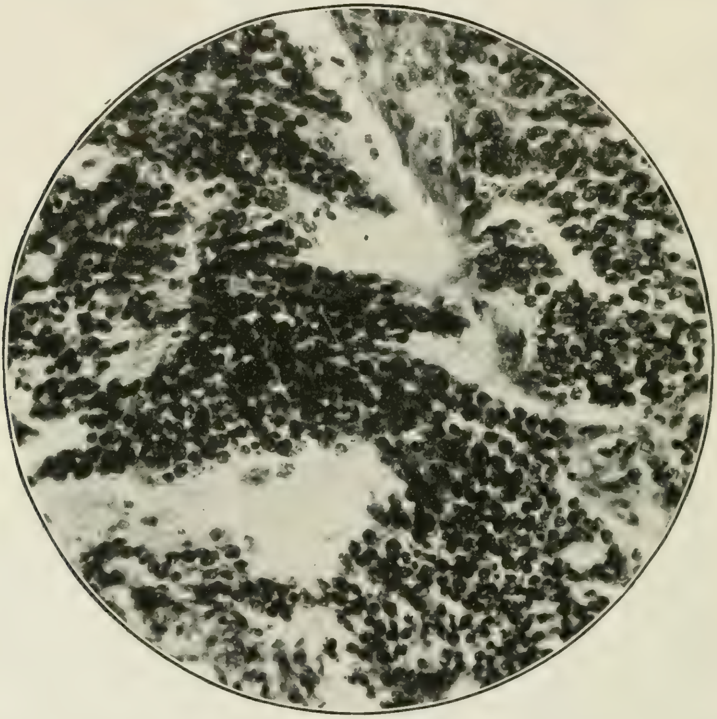

Fig. 7.—Photomicrograph, Case 3, showing bundles of fibrils between masses of the tumor cells and between the tumor and the stroma; about 400 diameters.

Sections through the upper pole of the kidney show a new growth consisting of large anastomosing columns of tumor cells with many mitoses and supported by a delicate connective tissue stroma. Most of the tumor cells are small and round. In many places there are elongated oval and pyriform-shaped cells. The latter have a finely granular cytoplasm which can often be traced out into long delicate processes. The nuclei are relatively large, vesicular in type and contain a large amount of chromatin in the form of a coarse network (Fig. 8). The amount of cytoplasm is very scanty and as a rule is eccentrically situated in relation to the nucleus. The size of the cells is slightly larger than the size of lymphocytes found in the germinal centers of lymphoid follicles. Here and there throughout the tumor there are very delicate fibrils occurring in small bundles between the tumor cells and extending between adjacent clumps of tumor cells (Fig. 7). These fibrils are also found in bundles of considerable size lying between the connective tissue stroma and the tumor cells. The fibrils are exceedingly delicate and have a granular structure and bear no resemblance to the deeply staining intercellular fibrils of connective tissue and neuroglia (Fig. 8). There is no rosette formation but the diagnosis of neuroblastoma sympathicum is established beyond question by the presence of the delicate nerve fibrils.

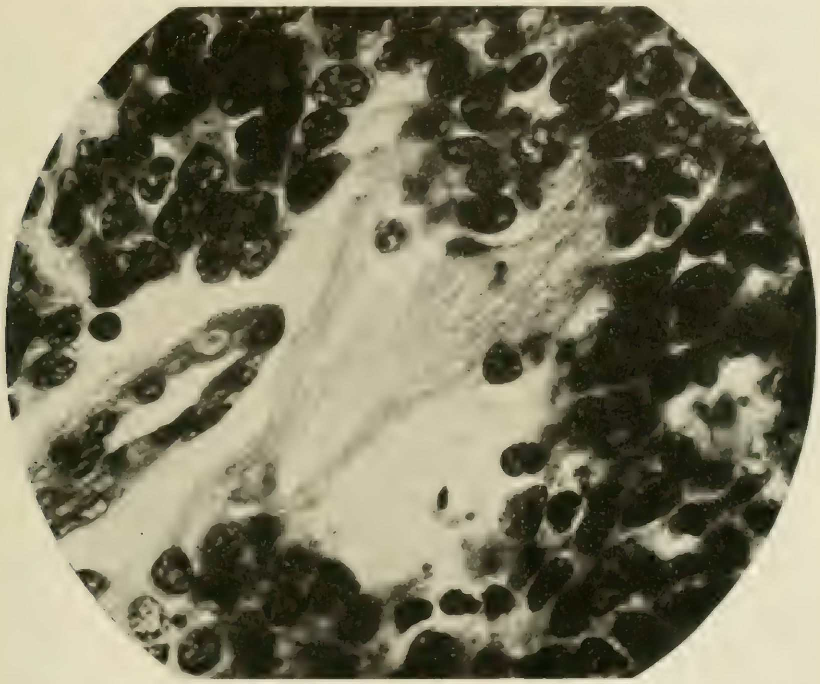

Fig. 8.—Higher power photomicrograph of a section from Case 3, showing the character of the nuclei and the fibrils; about 800 diameters.

No postmortem was obtained and therefore the location of the primary tumor cannot be proved. The extensive loss of substance and invasion of the kidney at the upper pole indicate, however, that the tumor took origin from the adrenal gland.

These three cases present the slight differences in the histology exhibited by this type of tumor. In the first case we have rosette formation in the primary tumor and in the metastases extreme rapidity of growth without rosette formation or fibril formation. The density of the nuclei is indicative of a large chromatin content and rapidity of growth, as has been noted by other authors. In the second and third cases no rosette formation was found. Fibril formation was abundant in the second case, less abundant in the third, which represents a type easily overlooked. These three cases bring the number of undoubted cases of neuroblastoma sympathicum to twenty-nine, of which twenty were primary in the adrenal gland. The others have taken origin in sympathetic ganglia (three), retroperitoneal tissues (three), coccygeal gland, nose and uterus. It is highly probable that many other cases of primary tumors of the adrenal gland reported as sarcomas were neuroblastomas, as, for instance, the fourteen cases of adrenal tumors with cranial metastases collected by Tileston and Wolbach.[11] Of all the cases reported, but one patient survived, Lehman's case,[9] the only successful operative removal of a tumor of this type in an infant.

Since a variety of terms have been used to designate the malignant tumors representing a primitive type of sympathetic ganglion cells, it seems advisable to indicate a choice. Wright's terms neurocytoma and neuroblastoma are too inclusive. Ganglioma embryonale sympathicum, introduced by Pick and Bielschowsky, has been regarded by several authors as unsatisfactory because of the employment of ganglioma by others to designate a more highly differentiated type of nerve cell tumor. Our own preference is for the term neuroblastoma sympathicum or sympathetic neuroblastoma.

REFERENCES

For the complete bibliography of this and related types of tumors the articles of Pick and Bielschowsky, Pick, Herxheimer, Wahl and Lehman should be consulted. The presentation of cases in the literature in tabular form by Wahl and by Lehman makes their papers particularly useful.

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[11] Tileston and Wolbach: Am. Jour. Med. Sc., June, 1908.

VARIATIONS IN THE LIPOID ("FAT") CONTENT OF THE BLOOD OF INFANTS UNDER CERTAIN NUTRITIONAL CONDITIONS *

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Clinical experience has shown that without a certain amount of fat in the food of an infant, normal growth is not be be expected. Excessively high fat feeding, on the other hand, may overtax the assimilative functions of the body and lead to most serious consequences. Thus intestinal indigestion with diarrhea and a lowering of the tolerance for all food is, at times, the result of an excessive amount of fat. Failure to gain weight, constipation, the conditions variously described as "Chronic Fat Indigestion," "Milchnährschaden," "Bilanzstörung," have all been attributed to relative or absolute excess of fat in the diet.

The infant fed on considerable amounts of fat, but unable to utilize this fat, is virtually in a state of fat starvation. Analyses of the stools for fat or its derivatives gives us some information as to the efficiency with which fat of the food is digested and absorbed. Further information as to the behavior of fat in the body of the infant can be obtained from a study of the fat of the circulating blood under varying conditions of feeding and states of nutrition.

If the fat of the blood represented only absorbed food fat on the way to the tissues, blood fat determinations would give us a reliable index of the amount of fat digested and absorbed. The process is not so simple, however, on account of the fact that the fat of the blood is derived from the tissues as well as from the food and there is no method at present available that will serve to differentiate the source of the fat. It has been shown that animals during complete and prolonged starvation may have as high a fat content of the blood as those fed on diets containing moderate amounts of fat.[1]

The reason for this is made clear when we consider the physiology of fat metabolism. Fat is absorbed largely by the mesenteric lymphatics and reaches the blood stream by way of the thoracic duct. There is reason for believing that this fat must be altered in some way; for example, the change from single to double bond linkages at places in

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* From the Boston Floating Hospital.

* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

[1] Bloor, W. R.: Jour. Biol. Chem., 1914, **19**, 1.

the fatty acid molecule,[2] before it can be "burned" in the body. The view at present most generally accepted is that these preparatory changes take place in the liver, and that whatever part of the ingested fat is immediately needed for fuel requirements is intercepted by the liver and converted into the combustible form. The remainder is transported by the blood to the fat depots of the body, in the subcutaneous tissues and elsewhere, and there deposited. These deposits may be drawn on from time to time as the body may require, and the fat transported by the blood stream back to the liver and subsequently burned.

It is thus evident why, during starvation, when the fat depots are drawn on, there may be considerable amounts of fat in the blood stream. If, however, fat is being burned in an efficient manner the amount in the blood stream would not be expected to rise to an excessively high point, and this, indeed, corresponds to the observed facts. As some fat is always being burned there is always fat in the blood, coming either from the intestine or from the fat depots. In normal adults the amount of fat does not vary greatly except following the feeding of considerable fat. If the fat were absorbed from the intestine at the same rate at which it was utilized in the body the blood fat percentage should not change very much. If fat absorption were more rapid than utilization, a high blood fat would result and the excess would be deposited in the fat depots.

A similar condition occurs when fat is drawn from the fat depots more rapidly than it can be utilized. This happens under certain pathologic conditions and the excess fat is deposited in the liver. In general, high fat in the blood means a deposition of fat somewhere in the body.

In order to interpret the analyses of blood for fat it is necessary to know the diet of the patient. An infant fed reasonable amounts of carbohydrate and protein would not be starving; consequently the fat depots would not be called on to as great an extent as during starvation. As a result, blood fat would not be as high as during complete starvation. If a certain amount of fat were added to the diet and none were absorbed, blood fat would remain low. With absorption, however, blood fat would be expected to rise. Hence, of two infants on the same feedings, the one digesting and absorbing fat would be expected to show the higher blood fat. Further, the one with the higher blood fat should be depositing fat in the subcutaneous tissues and other fat depots and therefore gaining weight. We have endeavored to determine if this is actually the case; that is, whether infants gaining weight have higher blood fat percentages than those who are stationary or losing in weight.

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[2] Leathes: The Fats, London, 1913.

The nutritional condition of an infant may be considered from two standpoints, the first of which has just been mentioned, and may be referred to as the nutritional *trend* or direction of the weight curve; the second, the nutritional *state*, or weight of the baby as compared with what his weight should be at his age. One of the striking differences between a well nourished and a poorly nourished infant is the amount of subcutaneous fat. Is this in any way proportional to the blood fat? We have investigated this question.

Methods of Study.—The infants investigated were patients in the wards of the Boston Floating Hospital. Most of the patients in this hospital were under 1 year of age and suffering from disorders of nutrition rather than from acute illnesses. Some infants recovering from mild ailments and the infants of wet nurses gave us the necessary "normals" for comparison. It was through the courtesy of Dr. Henry I. Bowditch, medical director, and Drs. Paul W. Emerson and E. W. Barron, visiting physicians, that we were given the opportunity to study the patients from their respective services.

Blood was obtained by venous or sinus puncture, and the fat (total lipoids) determined by Bloor's nephelometric method.[3] "Fat" determined by this method includes the higher fatty acids whether originally combined as neutral fats, as lecithin, or as cholesterol esters, and in addition all of the cholesterol. No effort was made to separate these individual components, as it seemed likely that the desired information could be obtained as well from the total fat determination.

In all, fifty-two determinations of blood fat from forty-eight different infants were made. In Table 1 is given the essential information concerning each case, together with the results obtained.

In the column headed "Nutritional State" (Table 1) the letters refer to the state of nutrition as determined by a comparison between the weight of the infant and the average weight of normal infants of the same age. The infants were arbitrarily divided into four classes as follows:

Class A, 85 to 100 per cent. of average normal weight.
Class B, 70 to 85 per cent. of average normal weight.
Class C, 60 to 70 per cent. of average normal weight.
Class D, below 60 per cent. of average normal weight.

In the column headed "Nutritional Trend" the signs refer to the general direction of the weight curve at the time of taking of the blood sample. Infants gaining in weight are classed as +, those stationary as ±, and those losing —. Feeding formulas are expressed roughly in

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[3] Bloor, Walter R.: Jour. Biol. Chem., 1914, **17**, 377. Part of the analytical work was performed in Dr. Bloor's laboratory in the Department of Biological Chemistry of the Harvard Medical School. We are greatly indebted to Dr. Bloor for his aid and helpful suggestions.

TABLE 1.—DATA OF AUTHORS' CASES

No.	Age in Mos.	Weight		Nutritional State	Nutritional Trend	Feeding			Calories per Kg.	Hours After Feeding	Blood Fat, per Cent.	Remarks
		Lb.	Oz.			Fat	Carb.	Prot.				
1	5	14	4	A	+	2.0	7.0	2.0	95	4	0.81	No disease
2	3	12	11	A	+	Breast fed			?	3	0.76	No disease
3	2	10	0	A	—	Breast fed			?	3	0.74	Syphilis; under treatment
4	18	21	4	A	±	0.0	4.5	3.2	45	3	0.66	Infectious diarrhea; convalescent
5	15	19	0	A	—	Buttermilk			65	4	0.66	Infectious diarrhea; acidosis
6	4	12	10	A	—	0.0	5.0	0.0	20	2	0.60	Intestinal indigestion; convalescent
7	18	21	0	A	—	Starving			0	12	0.57	Infectious diarrhea; acidosis
8	4	10	10	B	—	Starving			0	24	0.83	Severe diarrhea; acidosis
9	..	..	..	B	+	Breast fed			?	4	0.83	No disease
10	1	6	12	B	+	Breast fed			?	2	0.68	Syphilis; under treatment
11	6	13	4	B	—	Starving			0	36	0.67	Severe diarrhea; acidosis
12	10	14	6	B	—	0.0	5.0	0.0	50	2	0.52	Infectious diarrhea
13	2	7	9	B	—	1.2	5.4	1.0	65	2	0.52	Gastro-intestinal indigestion
14	1	5	14	B	—	Breast fed			?	4	0.60	Gastro-intestinal indigestion; mild
		5	7	C	+	Breast fed			?	4	0.77	Same child; recovered; week later
15	9	12	4	C	+	Breast fed			?	3	1.00	Pyelitis; convalescent
16	10	12	3	C	—	Starving			0	36	0.80	Severe diarrhea; acidosis
17	10	..	..	C	—	Starving			0	12	0.71	Severe diarrhea; acidosis
18	4	9	6	C	—	Starving			0	12	0.70	Severe diarrhea; acidosis
19	2	6	9	C	±	2.0	6.0	1.6	125	2	0.58	Intestinal indigestion; convalescent
20	3	7	8	C	+	2.0	6.0	1.6	125	3	0.64	No disease
21	1	5	14	C	+	1.4	6.0	1.2	100	3	0.64	Intestinal indigestion; convalescent
22	4	8	4	C	±	1.0	4.0	1.6	90	4	0.62	Syphilis; under treatment
23	2½	7	9	C	±	2.0	7.0	1.6	110	2	0.61	No disease
24	5	9	0	..	—	Protein milk			65	4	0.58	Intestinal indigestion
25	2½	6	14	C	±	Allm't mixte.			?	4	0.50	Intestinal indigestion
		7	0	C	+	Allm't mixte.			?	4	0.80	Same child recovered; week later
26	3	6	0	D	—	Starving			0	48	0.96	Severe diarrhea
27	4	8	7	D	—	Protein milk			40	2	0.71	Marasmus; nutritional edema
	4½	8	9	D	+	2.0	6.0	1.6	125	4	0.84	Same case; doing well
28	4	7	3	D	+	2.0	6.0	2.2	120	2	0.74	Syphilis; under treatment
29	11	12	0	D	—	2.0	6.0	1.6	100	4	0.73	No disease
30	3½	6	13	D	±	1.2	6.0	1.2	100	2	0.71	No disease
31	6	7	12	D	+	1.0	6.0	1.6	140	2	0.74	No disease
32	3½	7	7	D	±	2.0	6.0	1.6	110	2	0.71	No disease
33	2	5	14	D	—	Starving			0	12	0.52	Acute intestinal indigestion
	2½	5	5	D	—	1.0	5.0	1.2	90	4	0.70	Same case; recovering

TABLE 1.—DATA OF AUTHORS' CASES—(*Continued*)

No.	Age in Mos.	Weight		Nutritional State	Nutritional Trend	Feeding			Calories per Kg.	Hours After Feeding	Blood Fat, per Cent.	Remarks
		Lb.	Oz.			Fat	Carb.	Prot.				
34	4	..	..	D	±	0.4	2.2	1.6	...	2	0.70	No disease
35	12	9	6	D	+	0.0	4.5	3.2	75	2	0.70	Intestinal indigestion; convalescent
36	2½	..	..	D	—	Starving			0	.	0.70	Marasmus; moribund
37	6	9	0	D	—	1.6	6.0	1.2	120	2	0.70	Mongolian idiot
38	12	12	8	D	±	Soft diet			120	4	0.70	Anemia pseudoleukemica
39	3	5	4	D	±	Breast milk			120	4	0.70	No disease
40	3	6	8	D	+	2.0	7.0	1.6	125	2	0.67	No disease
41	2	5	8	D	—	Dil. breast milk			70	2	0.64	Marasmus
42	1	4	12	D	±	1.6	7.0	1.2	120	2	0.64	No disease
43	11	10	8	D	—	0.0	4.5	3.2	70	2	0.62	Rickets
44	10	9	11	D	±	Protein milk			125	2	0.61	Intestinal indigestion
45	3	6	5	D	—	3.0	5.0	1.2	125	4	0.65	Intestinal indigestion; convalescent
46	5	7	15	D	—	Buttermilk			50	3	0.60	Intestinal indigeston
47	5	7	4	D	—	Protein milk			70	3	0.58	Intestinal indigestion
48	7	11	14	D	±	2.0	6.0	2.8	120	4	0.52	No disease

percentages. The total food intake, in terms of calories per kilo, appears in a separate column and serves to indicate the amount of each formula taken during the twenty-four hours.

As indicated in the table, blood samples were drawn two, three, or four hours after the last feeding, excepting, of course, the infants who were starving. With one or two exceptions the infants studied were on a four-hour feeding interval.

Comparing different infants falling in the same general nutritional class and on similar diets, we were unable to detect any differences in the blood fat that could be attributed to the time of taking of the samples. This is easy to understand when we consider that fat digestion and absorption in the infant is a relatively slow process. The stomach is often not emptied until three hours after a meal, and even when feeding is at four hour intervals, fat absorption from the intestine must be an almost continuous process. Conditions in infants are vastly different from those obtaining in the dogs studied by Bloor.[1] These animals were fasted and then fed on pure olive oil. The blood fat rose gradually and reached a maximum at the end of about six hours. Had the animals been fed every four hours, the curves would have been expected to overlap and approach a continuous line. Furthermore, our infants were fed only on rather low fat percentages and on small total amounts as compared to the dogs.

Inasmuch as the taking of the blood sample does not seem to influence the blood fat percentage, in subsequent classifications in this paper no particular attention will be taken of the time interval. Furthermore, in each class of children studied, blood samples were taken at intervals which averaged approximately the same, therefore eliminating any effect of the time interval.

Nutritional state and blood fat.—In Table 2 the results on blood fat are arranged in groups according to the nutritional condition of the infants.

From the results (Table 1) it is apparent that *blood fat is independent of the state of nutrition of the infant.* Subcutaneous fat does not necessarily bear any relation to circulating fat. This is not surprising, as fat in the tissues represents fat deposited at some past time. A well nourished baby with plenty of subcutaneous fat may be losing weight and not storing up any fat; on the other hand, a thin baby may be laying on fat and have a blood rich in food fat on the way to the tissues. The important question in the nutrition of an infant is not so much whether he is fat or thin, but whether or not he is gaining weight.

TABLE 2.—Grouped Blood Fat Percentages

Nutritional State	A	B	C	D
Blood fat, per cent.	0.60, 0.74, 0.66, 0.81 0.66, 0.57, 0.76	0.83, 0.52, 0.52, 0.68 0.67, 0.60, 0.83	0.50, 0.80, 0.64, 0.80 1.00, 0.58, 0.71, 0.70 0.58, 0.64, 0.61, 0.77 0.62	0.70, 0.70, 0.73, 0.71 0.52, 0.70, 0.62, 0.58 0.70, 0.64, 0.74, 0.52 0.70, 0.74, 0.65, 0.71 0.84, 0.71, 0.67, 0.64 0.60, 0.61, 0.70, 0.96 0.70
Average	0.68	0.66	0.69	0.68

Nutritional trend and blood fat.—Considering the infants studied from the standpoint of their weight curves, and dividing them into groups, it is seen that infants gaining show, on the average, a distinctly higher blood fat than those whose weight is stationary or who are losing. The results appear in Table 3.

Particularly interesting are the results obtained on the blood of the same infant during gaining and during stationary or losing periods. (Table 1, Patients 14, 25, and 27).

In Table 3 are included *all* blood fat determinations that we have made. It may appear better to eliminate those patients who were fasting. If this is done the average for the stationary group becomes 0.63, and for the losing group 0.64, figures essentially the same as those obtained without eliminating the starving patients. In general, then, *an infant who is gaining weight, no matter what the state of his nutrition, will have a higher average blood fat than one who is not gaining.*

Blood fat and character of the feeding.—It is well known that infants are better able to "tolerate" the fat of breast milk than of cow's milk. If fat digestion and absorption are better when breast milk is fed, one might expect breast fed infants to show a high blood fat and a rapid gain in weight. In our group of infants who were gaining weight, those fed entirely, or in part, on breast milk showed an average blood fat percentage of 0.82, a considerably higher figure than any other group of infants in our series (Table 3). *Breast fed infants gaining weight have high blood fat percentages.*

TABLE 3.—NUTRITIONAL TREND AND BLOOD FAT

Nutritional Trend	Gaining			Stationary	Losing
	Breast Fed		Artificially Fed		
Blood fat, per cent.	0.83, 0.77, 0.68 1.00, 0.80		0.64, 0.70, 0.81 0.74, 0.74, 0.84 0.64, 0.67	0.70, 0.50, 0.71, 0.66 0.64, 0.52, 0.58, 0.71 0.76, 0.61, 0.61, 0.70 0.70, 0.62	0.73, 0.80, 0.52, 0.70 0.60, 0.62, 0.74, 0.58 0.70, 0.83, 0.58, 0.52 0.66, 0.52, 0.70, 0.65 0.71, 0.71, 0.70, 0.57 0.64, 0.60, 0.67, 0.96 0.60
Average	(0.82)	0.76	(0.72)	0.64	0.66

As none of the infants studied was on "top-milk" mixtures, we are unable to state the effect on the blood fat of feeding artificial formulae with high fat percentages. We did have, however, a number of infants on formulae containing little or no fat, and these showed a lower average blood fat than any other group of cases studied (Table 4).

An infant on a fat-free diet is absorbing considerable food and hence there is not as great a demand on the fat deposits as during com-

TABLE 4.—INFANTS ON FORMULAE CONTAINING LITTLE FAT

Character of Feeding	Fat Free	Starvation	Acidosis
Blood fat, per cent.	0.70, 0.70, 0.62, 0.60 0.66, 0.66, 0.52, 0.60	0.80, 0.52, 0.70, 0.83 0.72, 0.70, 0.57, 0.67 0.96, 1.02	0.80, 0.83, 0.72, 0.70 0.67
Averages	0.63	0.75	0.74

plete starvation; at the same time no fat is being absorbed, so that conditions favor a low blood fat.

During complete starvation blood fat figures are relatively high (Table 4, second column), as might be expected. The significance of this has already been discussed.

The majority of the infants starved were suffering from severe diarrhea; the general symptomatology approaching the clinical picture of so-called "intoxication." Five of these infants showed definite evidences of acidosis; there was hyperpnea, a lowering of the carbon dioxid tension in the alveolar air, and a diminution of the alkali reserve. The acidosis was of the type described by Howland and Marriott.[4] that is, an acidosis not due to the acetone bodies. It is interesting to note that, as a group, these cases of acidosis showed no higher blood fat than the group of starving infants without acidosis of a significant degree. It has been shown by Gray[5] that in diabetes a high blood fat percentage usually occurs with acidosis. It would seem likely that in infants of the type described the failure of blood fat to rise may be due to the peculiar nature of the acidosis, it being of an entirely different origin from diabetic acidosis.

It is interesting to note that the average blood fat of the forty-eight infants that we have studied is somewhat higher than the results obtained from normal adults by Bloor.[6] He found an average blood fat of 0.59 as compared with our figures of 0.68. Blood from the adults studied was drawn before breakfast and therefore the effect of feeding fat was eliminated, and at the same time the fast was not of sufficient length to use up the carbohydrate stores to such a great extent as to call out much fat from the fat depots. The figures that Bloor obtained might be considered minimum rather than average for the twenty-four hours. A further explanation of the differences lies in the fact that the adult is usually in a state of weight equilibrium, whereas the normal infant is gaining. The infant ingests more fat per unit of body weight than the adult, and would therefore be expected to have constantly more fat in the blood stream on the way from the intestine to the liver and fat depots.

The fact that certain groups of infants show amounts of blood fat which vary distinctly from the general average of other groups suggests the desirability of further and more intensive work on special types of nutritional disorders from the standpoint of blood fat. It would be of especial interest to study further the particular group of cases in which failure to thrive has been attributed to difficulties in the digestion and absorption of fats.

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[4] Howland and Marriott: Am. Jour. Dis. Child., 1916, **11,** 309.

[5] Gray, H.: Boston Med. and Surg. Jour., 1918, **178**, 16.

[6] Bloor: Jour. Biol. Chem., 1916, **25,** 577.

ACTIVE IMMUNIZATION OF INFANTS AGAINST DIPHTHERIA *

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The presence of diphtheria in civilized communities constitutes an important hygienic problem. It shows the need for a practical and efficient method of *active immunization,* that will protect the child and adult population. Such protection should be applied early in life, so that an efficient active immunity will be produced during that period when the individuals are most susceptible and the disease causes the greatest mortality; that is, from 1 to 5 years of age.

A. VITAL STATISTICS ON DIPHTHERIA

A short review of the tables furnished by vital statistics in this country, in England and in Germany will help to emphasize the foregoing statement, which is quite thoroughly realized by physicians in general, but especially by those engaged in public health work.

1. Morbidity Statistics.

TABLE 1.—Morbidity and Mortality from Diphtheria in New York City During the Past Five Years

Year	Morbidity	Mortality
1913	14,535	1,333
1914	17,129	1,491
1915	15,259	1,278
1916	13,521	1,031
1917	12,624	1,158
Total for five years	73,068	6,291
Yearly average	14,613	1,258

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2. Mortality Statistics.

TABLE 2.—MORTALITY FROM DIPHTHERIA IN NEW YORK CITY FROM 1891 TO 1900

Age	Number	Per Cent.
Under 1 year	1,665	9.2
1 to 2 years	4,263	23.0
2 to 3 years	3,817	21.2
3 to 4 years	2,900	16.1
4 to 5 years	1,908	10.6
Under 5 years	14,553	81.5
5 to 10 years	3,052	17.0
10 to 15 years	241	1.3
Under 15 years	17,846	

TABLE 3.—TOTAL MORTALITY AND MORTALITY UNDER FIVE YEARS FROM DIPHTHERIA IN NEW YORK CITY FROM 1901 TO 1917

Year	Total Mortality	Under Five Years	Per Cent.
1900	1,920	1,354	70.0
1901	2,068	1,546	74.7
1902	2,015	1,503	74.5
1903	2,190	1,606	73.3
1904	2,084	1,566	75.1
1905	1,544	1,178	76.3
1906	1,898	1,476	77.7
1907	1,470	1,354	92.1
1908	1,758	1,404	79.8
1909	1,714	1,418	82.7
1910	1,715	1,324	77.2
1911	1,281	1,004	78.3
1912	1,125	873	77.6
1913	1,333	972	72.9
1914	1,491	1,143	76.6
1915	1,278	967	75.6
1916	1,031	795	77.1
1917	1,158	842	72.7
Total	29,873	23,150	77.5

TABLE 4.—Mortality from Diphtheria in the United States. U. S. Special Report, 1900 to 1904

Age	Number	Per Cent.
Under 1 year	3,736	7.0
1 to 2 years	8,001	15.0
2 to 3 years	7,990	14.5
3 to 4 years	7,207	13.5
4 to 5 years	5,989	11.0
Under 5 years	32,923	61.0
5 to 10 years	14.818	27.6
10 to 15 years	3,191	6.0
15 years up	2,628	5.0
Unknown	87	
Total	53,647	

TABLE 5.—Mortality Census from Registration Area in the United States for the Year 1910

	Deaths	Deaths per 100,000 Population
1. Diphtheria	11,512	21.4
2. Measles	6,598	12.3
3. Scarlet fever	6,255	11.6

TABLE 6.—Mortality from Diphtheria in the Registration Area of the United States. U. S. Census 1914 and 1915

Year	Number	Deaths per 100,000 Population
1914	11,786	17.9
1915	10,544	15.7

TABLE 7.—Age Incidence of 2,711 Cases of Diphtheria Admitted to Baginsky's Children's Hospital in Berlin between 1890-1897.

Age	Number of Cases	Per Cent. of Total of Cases	Number of Deaths	Death Rate per 100 Admissions	Death Rate at Each Age Period
0 to 6 months	15	0.55	4	0.15	26.6
6 to 12 months	69	2.50	36	1.32	52.2
1 to 2 years	227	8.30	110	4.06	48.4
2 to 3 years	317	11.60	119	4.30	37.5
3 to 4 years	354	13.05	121	4.40	34.2
4 to 5 years	337	12.40	84	3.09	24.9
5 to 6 years	264	9.70	61	2.25	23.1
6 to 7 years	280	10.30	61	2.25	21.8
7 to 8 years	209	7.70	26	0.95	12.4
8 to 9 years	175	6.40	23	0.84	13.1
9 to 10 years	146	5.30	19	0.70	13.0
10 to 11 years	101	3.70	9	0.33	8.9
11 to 12 years	80	2.90	8	0.29	10.0
12 to 13 years	65	2.40	7	0.25	10.8
13 to 14 years	72	2.65	6	0.22	8.3
Total	2,711		694		Av. 25.6

TABLE 8.—Mortality from Diphtheria in England in 1915

	Number	Deaths per 100,000 Population
All ages	5,895	16.6
Under 15 years (same age group)	.....	49.4

These rates are about the same as in 1914, when the mortality was heavier than in any previous year.

The following facts may be deduced from the tables given:

1. That the morbidity and mortality from diphtheria is quite high and constant, showing that (*a*) in spite of the extensive use of small prophylactic doses of antitoxin the total number of cases of diphtheria has not been reduced to any extent; (*b*) the measures taken at present in isolating and treating the temporary or more persistent carriers of diphtheria bacilli are of little benefit in accomplishing results on a large scale.

2. That children from 1 to 5 years of age are most susceptible to the disease and show by far the greatest mortality. In one table 81.5 per cent. of deaths, in another table 77.5 per cent., are shown to have

occurred under 5 years of age. As is well known, the dangerous laryngeal forms and the complicating bronchopneumonias are seen especially in this group of young children.

3. That the mortality from diphtheria is nearly as great as that from measles and scarlet fever combined.

4. That the yearly mortality from diphtheria in the United States calculated on the basis of the figures given in Table 5 is about 23,540 and the morbidity from this disease would be approximately ten times higher. Such figures present themselves in spite of the very valuable therapeutic remedy which we have in the form of antitoxin. It would therefore be of the greatest importance, considering these impressive statistics, to utilize to the fullest extent possible a method of active immunization that will render our total infant population, as well as the susceptible portion of our child and adult population, protected against this disease.

Recent investigations into the subject of natural and active immunity in diphtheria,[1] and studies with the Schick test,[2] a valuable clinical test at our disposal at the present time for determining diphtheria immunity, would seem to offer a solution to the problem of the control of diphtheria.

The tables give the results with the Schick test on various groups of children. Tables 9 and 21 are interesting as showing the very large proportion of positive reactions among children over 6 months of age.

The protection of the infant derived from the mother is only temporary and lasts about six to nine months after birth. Some children retain this maternal immunity for a year, and some are protected for even one and one-half years. The period of greatest susceptibility to diphtheria is between the first and fifth years of life. After the sixth

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B. THE SCHICK TEST

TABLE 9.—Results with the Schick Test

Age	Total	Negative	Positive	Per Cent. Positive
6 mo. to 1 year	10	5	5	50.0
1 to 2 years	68	22	46	67.6
2 to 4 years	273	93	180	65.9
4 to 6 years	249	116	133	53.4
6 to 8 years	196	123	73	37.2
8 to 15 years	237	171	66	27.8
Over 15 years	167	126	41	24.5
Total	1,200	656	544	45.3

See also Table 21, summary of Schick tests at the New York Foundling Asylum.

TABLE 10.—The Schick Test at the New York Catholic Protectory

Age	Total	Negative	Positive	Per Cent. Positive
4 to 6 years	126	113	13	10.3
6 to 8 years	212	202	10	4.7
8 to 10 years	91	82	9	9.9
10 to 15 years	233	220	13	5.5
15 years and up	25	24	1	4.0
Total	687	641	46	6.7

TABLE 11.—The Schick Test at the Institute of Mercy

Age	Total	Negative	Positive	Per Cent. Positive
4 to 6 years	62	54	8	12.9
6 to 8 years	62	52	10	16.1
8 to 10 years	47	41	6	12.7
10 to 15 years	151	141	10	6.6
Total	322	288	34	10.5

TABLE 12.—The Schick Test at St. Joseph's Institute

Age	Total Tested	Immunes			Non-Immunes Positive	Per Cent. Positive	Per Cent. Pseudo
		Negative	Pseudo	Total			
a. (Boys)							
5 to 10 years	55	48	0	48	7	12.7	0.0
10 to 15 years	112	103	8	111	1	0.9	7.1
15 to 20 years	51	39	11	50	1	1.9	21.5
Total	218	190	19	209	9	4.1	8.7
b. (Girls)							
5 to 10 years	36	24	1	25	11	30.6	2.8
10 to 15 years	69	49	11	60	9	13.0	15.9
15 to 20 years	43	28	11	39	4	9.3	25.6
Total	148	101	23	124	24	15.5	16.2

TABLE 13.—The Schick Test and Control Test at the Dominican Convent

Age, Years	Total Tested	Immunes			Nonimmunes			Per Cent. Positive	Per Cent. Pseudo
		Negative	Pseudo	Total	Positive	Combined	Total		
4 to 6	52	29	8	37	14	1	15	28.8	15.4
6 to 8	67	46	14	60	6	1	7	10.4	20.8
8 to 10	32	13	12	25	4	3	7	21.8	37.5
10 to 15	71	42	25	67	2	2	4	5.6	35.2
Total	222	130	59	189	26	7	33	14.8	26.5

year the number of children showing a positive Schick reaction diminishes rapidly. Table 10 shows from 4 to 10 per cent. of positive reactors after the sixth year. Table 11 also shows a relatively small proportion of positive Schick reactions at this age (average 10.5 per cent.). Table 12 shows in a striking way that occasionally in an institution a group of 100 or more children over 10 years of age will be found, among whom only one or two may give a positive reaction. This will explain why diphtheria seems to be a relatively rare disease in some institutions, in which children from 7 to 15 years are congregated.

A prolonged experience extending over a number of years has shown to the writer the following important facts in connection with the Schick test and the active immunization with toxin-antitoxin:

1. The negative Schick reaction, when properly carried out with a suitable diphtheria toxin, indicates quite definitely the presence of immunity to diphtheria. This fact was conclusively demonstrated in our experience at the Willard Parker Hospital. During a period of over four years more than 1,200 patients suffering from scarlet fever were admitted to that institution, who gave on admission a negative Schick reaction. All the tests were made by the same observer, and the patients were carefully watched every day. None of these patients was immunized either actively or passively, and yet, even though from 15 to 20 per cent. became carriers of virulent diphtheria bacilli at one time or another during their stay in the hospital, not a single patient developed a true clinical diphtheria.

2. The negative Schick test is of value, not only in showing an immunity to diphtheria at the time the test is made, but also in indicating in children over 1½ to 2 years of age the *development* of a natural immunity, which seems to be *permanent*. This was quite definitely shown by making Schick retests on such children in the institutions in which we carried on our work in active immunization with toxin-antitoxin. Over 3,000 children, who had given a negative Schick reaction at the time of the first test, were retested at different intervals over a period of three years and the negative reaction was found to persist in almost all. From 1 to 2 per cent. gave a positive reaction at the retest, and these children can be regarded as borderline cases, who have a small amount of antitoxin that may show variations under different conditions.

3. In children below 6 to 9 months of age the immunity, as shown by a negative Schick reaction, is only temporary and derived from the mother through the placental circulation. In breast-fed infants antitoxic antibodies are also derived through the breast milk. Almost all these infants sooner or later become susceptible to diphtheria. Those whose mothers have no immunity of their own are susceptible

at birth, while most of the others, whose mothers are immune, become susceptible from six to nine months after birth. A few infants remain immune at 12 months, and an occasional child may remain protected by its maternal immunity even up to the eighteenth month. These facts came out very strikingly in our results at the New York Foundling Asylum. The results and the conclusions to which they lead in regard to the universal immunization of all children under 1 year of age or, to be on the safe side, under 1½ years of age, will be given further on.

4. The foregoing tables show that an increasing proportion of children gradually develop a natural immunity to diphtheria. In adult life the majority (85 to 90 and even 95 per cent.) have become immune. It is rather important to bear this fact in mind. It shows that by actively immunizing all children under 12 to 18 months, and only those children over 18 months who give a positive Schick reaction, we can render the child population immune to diphtheria and tide it over the period of greatest susceptibility. The following tables show that we can produce a lasting active immunity with diphtheria toxin-antitoxin in from 95 to 100 per cent. of susceptible individuals. This active immunity is shown by the fact that during subsequent exposure to the disease, the children remained free from diphtheria, and is also shown by our obtaining a persistent negative Schick reaction at later retests. This immunity has been found to last, now, over three years, and in a small group whom we had the opportunity of observing, over four years. These children will be retested further at yearly intervals to determine whether any number lose their active immunity. So far this has not been the case.

5. The character of the immunity produced by the injection of toxin-antitoxin may be either (*a*) an active immunity similar to that following other forms of vaccination, or (*b*) it represents the earlier development of a natural immunity that would have more gradually developed in these individuals in later years, or finally, (*c*) it represents a combination of these two factors. If it represented only the first type of immunity it would be likely only temporary and protect the child for about two or, at the utmost, only three years. If it repsented the second type, or natural immunity, it would be probably permanent. This is shown by the persistence for years of a negative Schick reaction in those children who are found naturally immune by the test. It is quite likely, however, that we are dealing with (*c*) a combination of these two factors. An active immunity is developed, and the tissue cells of the individuals are so sensitized that under subsequent conditions of exposure to the ubiquitous diphtheria bacillus they readily respond by producing a fairly large supply of antitoxin. This remains more or less constant in some, is found increased in others, and is

diminished slightly in still others. The following three tables represent determinations of the antitoxin content of actively immunized children. They show the amount of antitoxin produced and the variations in two examinations made at different times on the same persons.

C. ANTITOXIN DETERMINATION IN THE ACTIVELY IMMUNIZED

TABLE 14.—Two Antitoxin Determinations Made on Actively Immunized Children Six Months and Eleven Months after Two or Three Injections of Toxin-Antitoxin

(A) SHOWING A DIMINISHED OR A SIMILAR AMOUNT OF ANTITOXIN AT THE SECOND DETERMINATION

Number	Six Months, Units	Eleven Months, Units	Number	Six Months, Units	Eleven Months, Units
1	2.0	1.0	14	0.12	0.1
2	1.5	1.0	15	0.02	0.01
3	0.012	0.012	16	0.1	0.05
4	0.012	0.01	17	0.02	0.02
5	0.2	0.2	18	0.01	0.01
6	0.005	0.005	19	0.02	0.01
7	0.5	0.2	20	0.01	0.01
8	0.5	0.25	21	0.01	0.01
9	0.01	0.01	22	0.1	0.01
10	0.2	0.2	23	0.012	0.01
11	0.5	0.2	24	1.0	0.5
12	0.12	0.1	25	0.05	0.05
13	0.3	0.3			

(B) SHOWING AN INCREASED AMOUNT OF ANTITOXIN AT THE SECOND DETERMINATION

26	1.0	3.0	34	0.005	0.02
27	0.05	0.5	35	0.75	2.0
28	0.2	1.0	36	0.1	0.2
29	0.1	0.2	37	0.02	0.1
30	0.1	0.25	38	0.01	0.1
31	0.012	0.5	39	0.01	0.2
32	0.2	0.5	40	0.01	0.2
33	0.1	0.2			

The amount of antitoxin in Table 14 and in the following two tables represents units of antitoxin per cubic centimeter of serum. The determinations were made in the guinea-pig by a modification of Römer's intradermal test.

TABLE 15.—RELATIVE EFFICIENCY OF TWO AND THREE DOSES OF TOXIN-ANTITOXIN

Units of Antitoxin in Blood Serum	Group 1 2 Doses, Each 1.0 C.c. Number Injected	Group 2 3 Doses, Each 1.0 C.c. Number Injected
0.01	7	9
0.02	2	8
0.05	1	0
0.1	1	6
0.2	3	6
0.5	2	5
1.0	0	5
2.0 up	0	1
Total	16	40
Total showing 0.1 unit and up	6	23
Per cent. showing 0.1 unit and up	37.5	57.5

The results in Table 15 show that a better antitoxin production takes place after three than after two injections of toxin-antitoxin.

The next table (Table 16) shows the persistence of the active immunity, as determined by the presence of antitoxin in the blood from fifteen to eighteen months after the injections of toxin-antitoxin.

TABLE 16.—ANTITOXIN CONTENT OF ACTIVELY IMMUNIZED CHILDREN FIFTEEN TO EIGHTEEN MONTHS AFTER TOXIN-ANTITOXIN INJECTIONS

Units of Antitoxin	Institution			Total
	St. Dominic	Leake and Watts	St. Agnes	
0.005	7	4	..	11
0.01	5	13	..	18
0.02	8	7	..	15
0.05	16	5	..	21
0.1	9	5	7	21
0.2	13	13	1	27
0.5	15	16	13	44
1.0	2	1	13	16
2.0	4	2	7	13
4.0	3	2	9	14
8.0	5	1	0	6
Total	87	69	50	206
Total showing 0.1 unit and up	51	40	50	141
Per cent. showing 0.1 unit and up	58.6	60.0	100.0	53.9

Table 16 shows that a fairly large proportion of the immunized children have a considerable amount of antitoxin even as late as eighteen months after the injections of toxin-antitoxin.

D. ACTIVE IMMUNIZATION WITH DIPHTHERIA TOXIN-ANTITOXIN

The following tables show the immunizing results obtained with toxin-antitoxin, as determined by subsequent retests with the Schick reaction.

TABLE 17.—Retests after Active Immunization

(A) SUMMARY OF RESULTS OF ACTIVE IMMUNIZATION WITH DIPHTHERIA TOXIN-ANTITOXIN IN VARIOUS INSTITUTIONS

Institution	Total Tested	Doses of Toxin-Antitoxin	Months After Injections	Schick Results	Retest, Per Cent. Negative
1. St. Agnes..............	54	1 and 2	12	50— 4+	92.5
2. St. Dominic............	83	2 and 3	12	82— 1+	98.5
	19	1	4	13— 6+	68.4
3. N. Y. Juvenile Asylum..	82	3	12	80— 2+	97.8
4. St. Joseph's............	55	2 and 3	10	55—	100.0
	18	1	10	15— 3+	84.7
5. House of Refuge........	72	2 and 3	2.5	66— 6+	91.6
	56	1	2.5	48— 8+	85.7
6. Hebrew Inf. Asylum....	48	2	4	43— 5+*	89.8
	28	1	4	24— 4+*	85.7
7. Hebrew Orph. Asylum..	117	1	8	95— 22+	81.2
8. Leake and Watts.......	43	2 and 3	6	43—	100.0
	7	1	2.5	3— 4+	42.8
9. Colored Orph. Asylum..	91	3 750 units antitoxin	3	42— 49+	46.1
10. Skillman...............	150	2	2.5	142— 8+	94.6

* Received three more injections of toxin-antitoxin at this time. Schick retest at 10 months negative in all children.

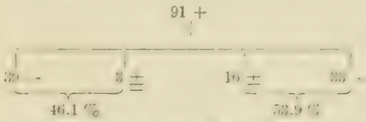
(B) FINAL RESULTS IN ACTIVELY IMMUNIZED CHILDREN

1. St. Agnes..............	20	1	20	18— 2+	90.0
	25	2	20	25—	100.0
	12	1	8	5— 7+	41.6
2. St. Dominic............	41	2	25	41—	100.0
	43	3	25	43—	100.0
3. St. Joseph's............	19	2	25	19—	100.0
	39	3	25	39—	100.0
4. Leake and Watts.......	49	3	17	48— 1+	98.0
	15	3	6	11— 4+	73.3
5. Colored Orph. Asylum..	68	3*	14	38— 20+	55.7
6. Institute of Mercy......	29	3†	12	28— 1+	96.6

* Received 750 units of antitoxin with first dose of toxin-antitoxin.
† Received 1,000 units of antitoxin with second dose of toxin antitoxin.

Table 17 shows the results of retests made from two and one-half to twenty-five months after the toxin-antitoxin injections. It shows in a striking way the high percentage of immunes, who received two or three injections of toxin-antitoxin. One injection was not as effective as the repeated injections. At the Colored Orphan Asylum we gave, in addition to the first dose of toxin-antitoxin, a prophylactic injection of 750 units of antitoxin. There was a small outbreak of diphtheria in the institution, which rendered it desirable immediately to protect the susceptible children. Table 18 gives the results in detail. It is interesting to see that a much smaller number of children became successfully immunized, thus showing a distinct interference by an excess of antitoxin with the efficient immunizing action of toxin-antitoxin.

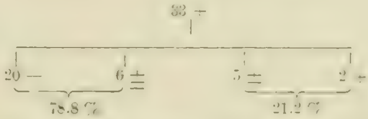
TABLE 18.—Results of Combined Active and Passive Immunization at the Colored Orphan Asylum



Schick retest made at three months. Three doses of toxin-antitoxin, each 1 c.c.; 750 units antitoxin with first dose.

In another institution, the Institute of Mercy, 1,000 units of antitoxin were given with the second injection of toxin-antitoxin. Table 19 gives the results of the first Schick retest.

TABLE 19.—Results of Combined Active and Passive Immunization at the Institute of Mercy



Schick retest at two and one-half months. Three doses of toxin-antitoxin, each 1 c.c.; 1,000 units of antitoxin with the second dose.

In this institution also the administration of an excess of antitoxin with the second dose of toxin-antitoxin has also interfered, though not to the same extent, with the efficiency of the immunizing response.

The active immunity following injections of toxin-antitoxin develops rather slowly. Such immunization alone, therefore, is unsuitable during a sudden, acute outbreak of diphtheria, when a considerable number of children have been exposed to the infection and have become carriers of virulent diphtheria bacilli. The danger from the disease to the non-immunes under such conditions is imminent. A combination of active and passive immunization of all positive Schick reactors would be indicated, to be followed by retests with the Schick reaction at the end of four to five weeks. If any of the children continue to give a positive reaction, showing that they had failed to become immune, they should receive three more doses of toxin-antitoxin at weekly intervals.

TABLE 20.—Time of Development of Active Immunity after Toxin-Antitoxin Injections

$$\begin{array}{c} 101\,+ \\ \underbrace{25\,- \qquad 5\,\pm}_{29.7\,\%} \qquad \underbrace{35\,\pm \qquad 36\,+}_{70.3\,\%} \end{array}$$

Schick retest at three weeks.

FURTHER SCHICK RETESTS ON THOSE WHO HAD SHOWN A POSITIVE REACTION AT THREE WEEKS

Number Positives Left	Time (Weeks)	Result		
43	4	2—	6±	35+
19	5	6—		13+
10	7	4—		6+
3	9	1—		2+
2	11	1—	1±	—

Table 20 shows a group of 101 children who were admitted to the scarlet fever pavilion of the Willard Parker Hospital. On admission they gave a positive reaction and were actively immunized with three doses, each 1.0 c.c., of toxin-antitoxin. A Schick retest was made at three week (one week after the third injection of toxin-antitoxin) and subsequently at weekly intervals during the remainder of their stay in the hospital. A certain number of patients were discharged from the hospital at the end of their period of quarantine, so that all children could not be retested to the end of three months. Yet the table shows clearly that the protection, while it develops slowly, is yet successful in most of the children. From the table it can be seen that at three weeks, of the 101 children, 30 had become immune, 71 still showing a positive Schick reaction. At four weeks, of the 71, 43 were left at the hospital, and of these 8 more gave a negative reaction. At five weeks, of the 35 non-immunes, 19 were left, and of these, 6 gave a negative Schick test. At seven weeks, of the 13 non-immunes, 10 were left, and of these, 4 gave a negative test. It can thus be seen that of the non-immunes that we were able to retest, the majority finally showed antitoxin production in from five to seven weeks after the first injection of toxin-antitoxin.

The toxin-antitoxin mixtures used for immunization should be slightly toxic and represent about 85 per cent. of an L + dose of toxin to each unit of antitoxin. The mixture should be prepared with a strong diphtheria toxin, so that each dose of 1 c.c. of the finished mixture will contain at least two and one-half almost neutralized L +

doses of toxin. Such mixtures may be prepared from a stronger toxin, so as to contain as high as five L+ doses, but a weaker toxin should not be used in its preparation. The mixture should be first tested in the guinea-pig by injecting 5 c.c. subcutaneously. The result should be a local induration and late paralysis, but not acute death of the animal.

E. OBSERVATIONS ON MATERNAL IMMUNITY TO DIPHTHERIA IN YOUNG INFANTS, AND ACTIVE IMMUNIZATION WITH TOXIN-ANTITOXIN

The following tables represent the results of studies at the New York Foundling Asylum on the duration of maternal immunity in young infants and on the efficiency of the immunization with toxin-antitoxin in infants and mothers, who gave a positive Schick reaction.

TABLE 21.—Summary of Schick Tests by Age Groups

Age	Total	Negative	Positive	Per Cent. Positive
0 to 6 months	101	82	19	18.7
6 to 12 months	84	40	44	52.3
1 to 2 years	52	28	24	46.1
2 to 4 years	127	82	45	35.4
4 to 6 years	108	88	20	18.5
6 to 8 years	25	22	3	12.0
Total	497	342	155	31.2

Table 21 shows that the largest proportion of positive Schick reactions was found between the ages of 6 months and 4 years. The positive reactions diminish rapidly after the fourth year of life.

TABLE 22.—Summary of Schick Tests and of Control Tests with Heated Toxin on Children and Adults

Age	Total Tested	Immunes			Nonimmunes			Per Cent. Positive	Per Cent. Pseudo
		Negative	Pseudo	Total	Positive	Combined	Total		
Children 0 to 8 years	519	354	23	377	140	2	142	27.3	4.4
Adults.........	113	59	43	102	6	5	11	9.7	38.0
	632			479			153		

In Table 22 it is interesting to note the relatively small number of pseudoreactions in children up to 8 years of age (4.4 per cent.), and the relatively large number in adults (38.0 per cent.), as compared with the positive Schick tests, of which the children (27.3 per cent.) have nearly three times as many as the adults (9.7 per cent.

TABLE 23.—Comparative Results with Schick Test in Mothers and Infants

Ages of Infants, Months	A Mother Neg. Infant Neg.	B Mother Neg. Infant Pos.	C Mother Pos. Infant Pos.	D Mother Pos. Infant Pos.
Up to 3	18	1	4	0
3 to 6	19	2	2	0
6 to 9	9	11	1	0
9 to 12	2	10	0	0
12 to 15	4	6	0	0
15 to 24	2	2	0	0
Total	54	32	7	0

Table 23 shows the following interesting points:

(*a*). The antitoxin immunity of the infant obtained from the immune mother lasts for about six to nine months after birth. Column A shows that thirty-seven out of fifty-four, or 68.5 per cent., had a negative Schick test during the first six months of life. The negative reaction in the nine children between 6 and 9 months of age is probably also due to a continuation of the passive immunity derived from the mother, while in the remaining eight children we may or may not be dealing with such an immunity. Only repeated Schick tests at later intervals could determine this point. The children who were still passively protected would lose their antitoxin in the course of the next few months, and then give a positive reaction; while those whose negative Schick reaction indicated an early developed natural immunity would continue to show a negative reaction.

(*b*). Column B shows that a large proportion of children belonging to immune mothers have positive Schick tests after the sixth month of life. Twenty-seven out of thirty-two children between 6 and 15 months, or 84.3 per cent., gave a positive Schick reaction.

(*c*). In Column C seven children are shown who gave a positive reaction and whose mothers also gave a positive reaction to the Schick test. The results indicate definitely that where a mother has no immunity, none will be present in her infant, if it is below 6 months of age.

(*d*). Column D shows that no case was found in which the mother had a positive and her young infant a negative Schick reaction. It was, of course, to be expected that where the mother had no immunity, none would also be found in her infant.

TABLE 24.—Schick Test and Retest at 6.5 Months in Mothers and Infants. Active Immunization with Toxin-Antitoxin

Group 1 No.	Mother Immune			Infant Immune				
	Mother	Test 2/5	Retest 8/21	Infant	Age	Test	Age	Retest
1	A. G.	Ps. —	Ps. —	A. G.	1 mo.	—	7 mo.	+
2	L. W.	Ps. —	Ps. —	F. W.	4 mo.	—	11 mo.	+
3	A. S.	Ps. —	Ps. —	J. S.	5 mo.	—	12 mo.	+ +
4	B. S.	—	—	A. S.	6 mo.	—	12 mo.	±
5	A. C.	—	—	J. C.	4 mo.	—	11 mo.	+
6	B. C.	Ps. —	Ps. —	R. C.	5 mo.	—	12 mo.	—*
7	M. C	Ps. —	Ps. —	C. C	6 mo.	—	13 mo.	+
8	M. L.	—	—	M. L.	5 mo.	—	12 mo.	—
9	C. B.	—	—	H. H.	2 wk.	—	7 mo.	±
10	C. M.	—	—	E. M.	3 mo.	—	10 mo.	+
11	W. F.	—	—	R. F.	2 mo.	—	8 mo.	+
Group 2	Mother Immune			Infant Susceptible. Toxin-Antitoxin				
12	J. E.	—	—	M. E.	8 mo.	+ +	14 mo.	—
13	M. R.	—	—	G. R.	8 mo.	+	15 mo.	—
14	S. C.	Ps. —	Ps. —	J. C.	6 mo.	+	13 mo.	—
15	R. K.	Ps. —	Ps. —	E. K.	7 mo.	+	14 mo.	—
16	C. C.	Ps. —	Ps. —	T. C.	6 mo.	+	13 mo.	—
Group 3	Mother Susceptible Toxin-Antitoxin			Infant Susceptible. Toxin-Antitoxin				
17	M. M.	+	—	E. M	1 mo.	+	7 mo.	—
18	G. W.	Ps. +	Ps. —	E. W.	6 wk.	+	7 mo.	—
19	A. W.	Ps. +	Ps. —	A. W.	5 mo.	+	12 mo.	—
20	V. P.	+	—	G. P.	5 mo.	+	12 mo.	—

Ps. — = Pseudoreaction in an immune mother.
Ps. + = Pseudoreaction and positive reaction or combined reaction in a susceptible mother.
* Marasmus.

Table 24 shows in a striking way the following points:

1. In Group 1 there are eleven mothers and their infants, both of whom gave a negative Schick reaction at the time of the first test. The age of the infants at this time was 6 months or under. When

retested 6.5 months later, all but two of the infants gave a positive Schick reaction. One of the two (No. 6) was marasmic at the time of the retest. No. 4 was slowly losing its maternal immunity at 12 months, No. 7 was beginning to lose it at 6 months and had completely lost it at 13 months. No. 9 was just beginning to lose its maternal immunity at 7 months.

This group as well as the following two groups also show that the infant does not inherit the hypersensitiveness of the mother to the bacillus protein, which she shows in the form of pseudoreactions.

2. In Group 2 there are five mothers who were immune and gave a negative Schick reaction. Their infants, 6 months of age or over, were susceptible and gave a positive reaction. The infants were actively immunized with three doses, each 0.5 c.c. of toxin-antitoxin. At the retest 6.5 months later all gave a negative Schick reaction, thus showing that they had been successfully immunized.

3. In Group 3 there are four susceptible mothers whose young infants were also susceptible. All gave a positive Schick reaction at the primary test. To the mothers three doses of toxin-antitoxin, each 1 c.c., were given; to the infants three doses, each 0.5 c.c. At the retest, 6.5 months later, both the mothers and their infants gave a negative Schick reaction, thus showing that they had all become actively immunized.

4. The table shows very definitely that almost all infants, if they are not already susceptible at birth, become susceptible to diphtheria within the first year of life. Only a few infants retain their maternal immunity after the twelfth month, and probably all lose it before the eighteenth month of life.

5. The results show the efficiency of the active immunization with toxin-antitoxin.

6. From the table it can also be seen that a large proportion of mothers, ten out of twenty, gave a pseudoreaction. These pseudoreactions are best determined[3] by making a control test on the opposite forearm with a dilution of diphtheria toxin which has been heated at 75 C. for five minutes. In the control dilution 50 per cent. more of the heated toxin is used; the excess is added to allow for any possible deterioration that may have taken place in the bacillus protein during the heating process. It is this substance which causes the pseudoreactions.

7. The toxin-antitoxin injections produced *very little local or con-*

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[3] Zingher, Abraham: The Pseudo-Reaction in the Schick Test and Its Control, Jour. Am. Med. Assn., 1916, **66,** 1617. Zingher, Abraham: The Schick Test among Troops of the National Army, Jour. Am. Med. Assn., 1918, **70,** 227.

stitutional disturbances in these young infants. It is this freedom also from any marked reactions to the injections that makes the immunization in early life a very desirable procedure. Some of the mothers, especially those showing pseudoreactions, had rather severe local and constitutional symptoms, consisting of redness, swelling and tenderness of the arm, headache and slight febrile disturbance, lasting about two days. This susceptibility of older individuals is due, as stated before, to the bacillus protein contained in the mixture.

SUMMARY AND CONCLUSIONS

1. *All infants below 12, and if possible below 18, months of age should be actively immunized with three doses, each 1.0 c.c., of toxin-antitoxin. These injections should be given irrespective of the Schick test the infants may show at the time of immunization.* The injections are given subcutaneously in the arm or below the angle of the scapula, and repeated every seven days. The toxin-antitoxin is well tolerated by young infants, and for that reason the dose advised is the same as that given to older children. The relatively larger dose of toxin-antitoxin will, of course, also give rise to a better immunizing response.

2. All children over 18 months of age, as well as all youths and adults, should be tested with the Schick reaction first, and only those giving a positive reaction immunized with toxin-antitoxin. Three injections, each 1.0 c.c., are given subcutaneously, one week apart.

3. In infants below 18 months of age the Schick test is not a necessary part of the immunization, since all the infants should be actively immunized. By omitting the Schick test the procedure is greatly simplified for many general practitioners, to whom the test even now appears as a difficult and complicated procedure. The greater part of the most effective prophylaxis against diphtheria still remains in the hands of the general practitioner, and it will be only by getting his interested cooperation in this work and facilitating the process of immunization for him, that results of any magnitude will be achieved. Whenever possible, however, it will be of scientific interest to apply the Schick test to the infants as well as to the older children and adults.

4. The toxin-antitoxin mixture should be prepared in a reliable laboratory and carefully tested for potency in the guinea-pig before it is sent out for use. The mixture used should be slightly toxic and should represent about 85 per cent. of an L+ to each unit of antitoxin. It is important that the toxin-antitoxin should be supplied free of charge to physicians by municipal and state departments of health, so that immunization on a large scale will be carried out. For the

Schick test the outfit[4] devised by the writer will be found very convenient.

5. Improvements in the method of immunization are possible, and further work is being carried out at present especially to see whether a single dose of toxin-antitoxin will give in a considerable number of these infants results as good as those obtained with three doses. This would undoubtedly simplify the process and make it very convenient for general use. Our own results with single doses in a limited number of children have not shown as high a percentage of successful immunizations as those obtained by multiple injections.

6. The active immunization against diphtheria should be carried out first of all by the private physicians in the different homes, where a majority of the infants can be reached. In larger centers of population the milk stations, day nurseries, children's dispensaries, infant and orphan asylums furnish large groups of children suitable for immunization. The children of preschool age found in kindergartens and those of school age should be tested first with the Schick reaction, and those giving a positive test actively immunized. Whether such procedure can be made compulsory in the schools will depend on the enlightenment of the community, in which the work is to be carried out. Adults, especially those frequently or constantly exposed to diphtheria, such as doctors, nurses, hospital orderlies and patients in contagious disease hospitals, should also be tested with the Schick reaction and those giving a positive reaction actively immunized.

7. Finally, it may be stated that the diphtheria problem would seem nearer a solution now by the thorough application of these newer diagnostic and immunizing procedures, which should be encouraged by the various departments of health.

This work was carried out under the direction of Dr. William H. Park, Director of the Research Laboratory of the New York City Department of Health. His interest in the problem of diphtheria has been a great stimulus in continuing this study over a period of years.

The Research Laboratory will supply at a very reasonable price the toxin-antitoxin for immunization and the toxin for the Schick test. Where necessary the material will be supplied free of charge on condition that full reports will be sent in on blanks furnished by the laboratory. The toxin-antitoxin can now also be obtained from Parke, Davis & Co.

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[4] Zingher, Abraham: A Simple Outfit for the Distribution of Diphtheria Toxin for the Schick Test, Jour. Am. Med. Assn., 1915, **65**, *329*.

INFANTILISM, WITH TWO CASES OF THE BRISSAUD AND THE FRÖLICH TYPES, RESPECTIVELY *

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The subject of infantilism has come in recent years into ever increasing prominence. The term should be applied not only to adolescents or adults who possess in some degree the bodily and often the psychic characteristics of infancy, but to children of any age in whom there is a persistence of characters, especially sexual, which belong to a period of life decidedly earlier than the actual age of the patient. Further, a sharp distinction should be drawn between infantilism and nanism. There may be dwarfs who are in no respects infantile, such as those of a rachitic or achondroplastic nature. As Hastings Gilford[1] has pointed out, there has been in them an arrest of *growth*, but not of *development*. Less often there may be cases of infantilism which are the reverse of being dwarfs, as in one of the instances which I desire to record.

Much confusion still exists, however, in the classification of forms of infantilism. That proposed by Hastings Gilford[1] is worthy of serious consideration. The cases are divided by him into the essential forms, including ateleiosis and progeria; and the symptomatic forms, including the Lorain and the Brissaud types. Other forms of symptomatic infantilism have been described; among them the intestinal, pancreatic, pituitary, renal, cardiac and lymphatic forms.

It is not the intention, however, to review the subject at length in this connection, but merely to report two instances of the Brissaud and the pituitary types, respectively. They are put on record not only on account of their intrinsic interest, but because in some respects they were studied with considerable care.

REPORT OF CASES

Case 1.—Mary G., aged 7 years, Italian, entered the children's ward of the hospital of the University of Pennsylvania, Jan. 23, 1912. The family history was negative, the parents and grandparents having been apparently normal in development. Five other children were living and well and in normal condition. The father had some asthma, but in other respects had good health.

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* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

[1] Gilford, Hastings: Lancet, London, 1914, **1**, 587.

The child was well during infancy and breast-fed up to the age of 21 months. When 1½ years old she had a severe attack of whooping cough lasting six months, exhibiting spasms of coughing in which she would often fall to the floor, "looking as if she were dead." Since that time she is said not to have grown any physically, although mentally the parents think she is normal. She frequently cries and complains of pain before rain or damp weather. She also appears to be a trifle weak in her legs at times. A year prior to admission she was examined by Dr. J. W. McConnell of the Department for Nervous Diseases, who found the mental condition apparently normal.

Examination.—A well nourished Italian child. The extremities seem short for the size of the thorax, and the legs are slightly bowed. The skin is harsh and dry, with a tendency to gooseflesh. The child talks plainly and coherently, answering questions rationally, as far as can be determined, but she speaks chiefly Italian. She seems strong for her size, but walks with a slight wabbling gait. Her weight is 20 pounds (normal for the age, 49 pounds); her height 29 inches (normal for the age, 45 inches). Expressed relatively, this child at 7 years has the weight belonging to one of 10 months, and the height of one of 20 months. The head is rather large and well formed; the hair short and slightly dry and harsh. No enlargement of the cervical lymphatic glands is noted, nor any rigidity of the neck. The eyes are somewhat far apart; the palpebral fissure narrowed, but without slanting of the eyes. The tongue appears slightly larger than normal, but does not protrude. Examination of the nose, ears and pharynx gives negative results. The thyroid gland cannot be palpated, and this region in the neck does not seem to be as full as in normal children. The chest is short and full. There are slight subcutaneous fatty deposits in the supraspinous fossae. There is no enlargement of glands in the axilla. The heart and lungs appear to be normal; there is no beading of the ribs; the abdomen is much distended, resulting in a distinct costal flare, and producing a compensatory lordosis of the lumbar spine; no masses can be felt in the abdominal cavity; the spleen cannot be felt, and the liver is not enlarged. Nothing wrong is discoverable in the extremities other than the shortness and bowing referred to.

January 24 measurements were taken of different parts of the body, contrasting these with similar measurements of a boy of the same age in the hospital at the time. The measurements of the patient were taken again on June 7, and are shown in the third column in the tabulation.

MEASUREMENTS

	Normal Boy, Jan. 24, Inches	Marie, Jan. 24, Inches	Marie, June 7, Inches
Height	48	29	30¼
Dorsal spine to iliac crest	11½	8	8½
Dorsal spine to floor	38	21½	22½
Anterior superior spinous process to external condyle	13¼	7¼	7¾
Anterior superior spinous process to external malleolus	24	13¼	14
Arms	15½	8	8½
Hands	5½	3½	3¾
Fingers	2½	1¾	1¾
Suprasternal notch to symphysis	15½	11	11½
Suprasternal notch to floor while standing	39	21	23¾
Suprasternal notch to glabella	18¾	15¼	17½

The contrast in size is well shown in the accompanying photograph (Fig. 1).

The patient while in the hospital was cheerful, active, and seemed to be of good mentality, as far as could be judged in a child of foreign parentage with a limited knowledge of English. The temperature averaged somewhat below normal—from 97.5 to 98 F. She was troubled at times with cough, which yielded to treatment, and early in June it was noticed that she was perspiring a good deal about her head. Apparently she did not have this condition earlier, and it may have been the result of treatment. The bowels were regular, formed or soft, brownish in color. Bacteriologic examination made on June 9 showed the stools negative for *Bacillus bifidus, Bacillus infantilis,* coccal and fermentative forms. Roentgen-ray examination of the body made by Dr. Henry K. Pancoast revealed nothing abnormal. The blood examined on admission gave hemoglobin, 58 per cent.; red blood corpuscles, 3,440,000; leukocytes, 11,000; with polymorphonuclears, 69 per cent., and lymphocytes, 21 per cent. The last examination, on June 9, showed hemoglobin, 70 per cent.; red blood corpuscles, 4,000,000; leukocytes, 8,000, with polymorphonuclears, 36 per cent., and lymphocytes, 45 per cent. Examination of the urine made on several occasions showed a faint trace of albumin, and at times a few cylindroids and casts, but no indication of any disease of the kidneys.

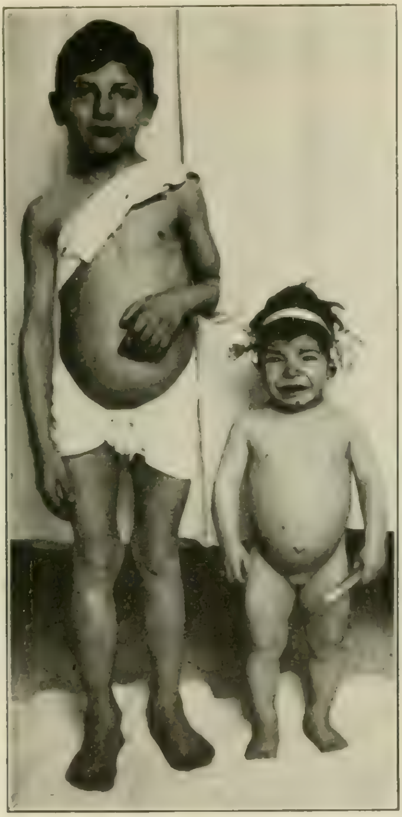

Fig. 1.—Infantilism of Brissaud type; patient beside a normally developed boy of the same age.

Thyroid extract was first administered in doses of one-half grain three times a day, and continued until March 31, when it was increased to 1 grain three times a day. This was persisted with until May 3. Meanwhile there had been at first a moderate loss in weight, followed by a slight gain; so that on May 3 she had lost in all about a pound. There had been, meantime, a slight but noticeable increase in the size, as is shown in the measurements taken on June 7. On May 3 the thyroid extract was discontinued and pituitary extract given until May 27 in doses of 1 grain three times a day. She left the hospital June 16 weighing 21 pounds.

This case was at first supposed to be intestinal infantilism, and the provisional diagnosis to this effect was recorded on the case-history. Further study seemed, however, to negative this diagnosis. There was not the general poor health, emaciation, anemia and disturbance of the gross character of the stools seen in this disease; and bacteriologic examination of the feces showed, as stated, an absence of the *Bacillus bifidus, Bacillus infantilis* and coccal forms, which, according to Herter, are present in intestinal infantilism. On the other hand, certain features existed which were very suggestive of infantilism of the Brissaud type. There were, namely, the moderate harshness of the skin, the bowing of the legs, the prominent abdomen, the moderate deposits of fat over the scapulae, and the like, all of which pointed to a hypothyroidism; not, it is true, of a degree to produce cretinism, but at least to make the subject cretinoid. The roentgen examination reported negative findings. Certainly there was nothing of a nature about them to suggest achondroplasia, nor were there, indeed, any other symptoms characteristic of this affection.

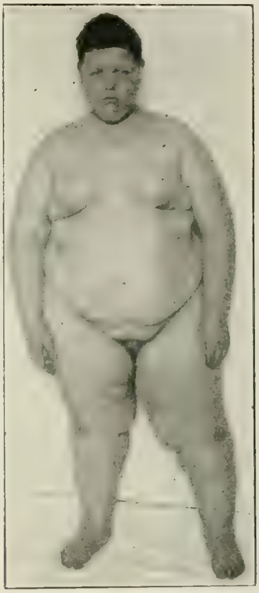

Fig. 3.—Pituitary infantilism.

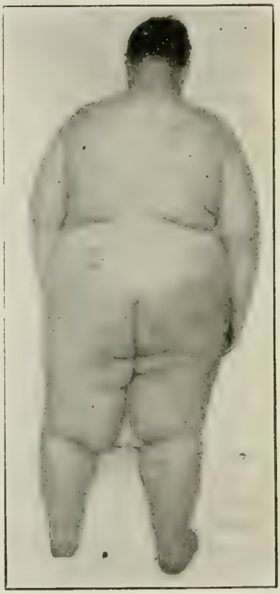

Fig. 2.—Pituitary infantilism.

CASE 2.—John S., aged 11 years; admitted to the Children's Ward of the Hospital of the University of Pennsylvania, Feb. 7, 1915, for excessive obesity. The parents stated that the tendency to the undue deposit of fat had been noticed since the age of 11 months. This had been gradually progressing and did not seem to be influenced by diet. The health in other respects had been good, and his mental capacity rather above the average, they thought. He had always indulged in a fair amount of exercise. The father said that the boy had had a fall when 14 months old, to which he attributed the existence of a limp. Both parents are stout, but not to any abnormal degree; one brother and one sister said to be "plump," but not excessively fat.

Examination.—The boy is unusually large for his age (Figs. 2 and 3), and excessively obese. The breasts are large, apparently from deposit of fat; the thyroid gland cannot be felt; there is nothing abnormal about the heart, lungs, or abdomen. He appears to have the full intelligence of a boy of his age. The following measurements were taken: height, 5 feet 1 inch (normal for age, 4 feet 5 inches); weight, 251 pounds (normal for age, 70 pounds); circumference at nipples. 45½ inches; just below this, 44 inches; at umbilicus, 47 inches; at anterior superior spinous processes, 51 inches; of left thigh, 34 inches; right thigh, 33 inches; calves, 21 inches; ankles, 11 inches; arms, 15½ inches; left forearm, 12 inches; right forearm, 12½ inches; left wrist, 8 inches; right wrist, 7½ inches. In brief, this boy at 11 years has the height of one of between 14 and 15 years, and a weight beyond that of a normal man.

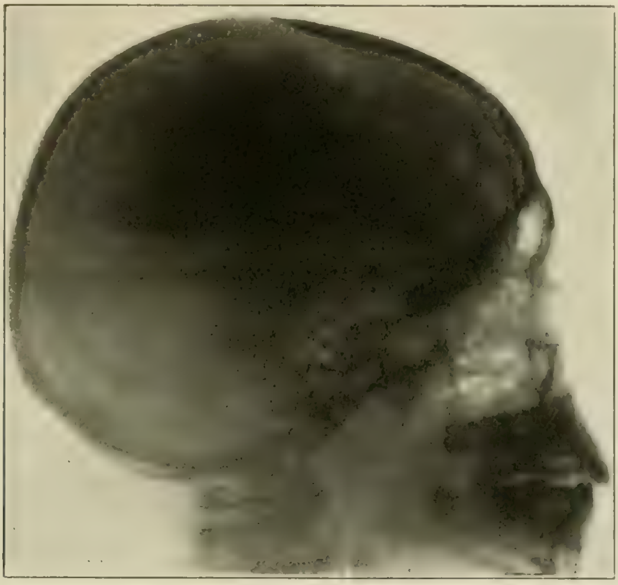

Fig. 4.—Pituitary infantilism; roentgenogram of skull showing small sella turcica.

The boy walks with a distinct limp. The abdomen is very pendulous. The penis is buried in fat, but seems to be small for his age and very small for the rest of his development. The testicles are descended, but are very small. There is almost no trace of pubic hair.

The blood contained 4,740,000 red blood cells; 8,600 leukocytes; 80 per cent. hemoglobin; polymorphonuclears, 76 per cent.; lymphocytes, 19 per cent.; large mononuclears, 4 per cent.; eosinophils, 1 per cent. The urine shows specific gravity, 1.022; slight trace of albumin; no formed elements. Dr.

Henry K. Pancoast made a roentgen-ray examination of the head (Fig. 4) and reported "sella turcica definitely smaller than normal, indicating a small pituitary body." An examination for the sugar tolerance made by Dr. A. H. Hopkins on February 12 resulted as follows: preformed sugar, 0.084; 100 gm. of glucose given by mouth showed:

½ hour after ....blood-sugar = 0.088
1 hour after ....blood-sugar = 0.104
1½ hours after ....blood-sugar = 0.090
2 hours after ....blood-sugar = 0.090
3 hours after ....blood-sugar = 0.106
4½ hours after ....blood-sugar = 0.086

No glycosuria occurred throughout.

A test for sugar tolerance was again made by Dr. Hopkins on April 19, after continued administration of pituitary extract during two months. This gave: preformed sugar, 0.060; 100 gm. of glucose given by mouth:

½ hour after ....blood-sugar = 0.110
1 hour after ....blood-sugar = 0.189
1½ hours after ....blood-sugar = 0.2
2 hours after ....blood-sugar = 0.151
3¼ hours after ....blood-sugar = 0.142

Fehling's solution was decolorized at the end of 1 hour, 1½ hours and 2 hours. The test showed marked reduction in the sugar tolerance after the administration of pituitary extract. Examination by Dr. Edward Martin indicated that the limp in the left leg depended probably on a coxa vara.

The patient was given a low carbohydrate diet in limited amounts. On March 12 he was ordered a special diet of known quantities, starting with four eggs (180 gm.), milk (1,000 c.c.), cream (50 c.c.), bread (200 gm.), butter (50 gm.), cream of wheat (200 gm.), sugar (16 gm.). This was varied from time to time to a slight extent, and meanwhile the child was made to exercise systematically in the hospital gymnasium. It is likely that he did not confine himself strictly to his diet, but ate other articles surreptitiously. In any event he was taken home May 30, having lost only 17 pounds.

This case represents an excellent instance of the hypopituitarism of Fröhlich, except in certain particulars. The infantile character of the sexual organs, the great obesity and its distribution, the tolerance for carbohydrates are positive indications. On the other hand, the subjects of Fröhlich's syndrome often exhibit a retarded skeletal development, while the case now reported possessed a decided overgrowth. This may depend, as Cushing has suggested, on activation of the anterior lobe of the pituitary body combined with insufficiency of the posterior lobe. The excessive action of the anterior lobe is the condition which, developing later in life, would result in acromegaly, but appearing earlier, as Brissaud suggests, produces gigantism. My patient was certainly of gigantic proportions for his age. Whether further growth would continue cannot be known. I regret that no roentgen ray studies were made of the developmental condition of the bones.

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INTRATHECAL INJECTION OF HORSE SERUM IN THE TREATMENT OF CHOREA

A PRELIMINARY STUDY OF SEVEN TREATED CASES *

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The clinical picture of chorea has never been more succinctly drawn than it was by Sydenham, who first described it as a clinical entity. Little was added to our conception of the disease until the middle of the nineteenth century, when the French clinicians made it a matter of particular study, and later German clinicians and Americans, especially Weir Mitchell and Osler, did much to separate the malady from similar nervous diseases. Later Osler was especially active in attempting to reach the etiology of the disease, together with Stephen MacKenzie he was instrumental in emphasizing the relation of chorea to manifestations of the group of symptoms then known as rheumatism, although as early as 1866 Germain See had insisted on this relationship. MacKenzie was able to relate less than 30 per cent. of his cases of chorea to rheumatism, and later observers, notably Morley Fletcher and Hughes, record similar findings.

With the increasing influence of bacteriology came a suspicion on the part of the medical profession that chorea was an infectious disease. The striking and well authenticated findings of Poynton and Paine, who demonstrated a diplococcus which they claim is etiologic in cases of rheumatic arthritis and endocarditis, and the earlier and somewhat similar findings of Wassermann and Westphal led to a further investigation of the relationship between these two diseases, and the former observers reported the presence of their diplococcus rheumaticus in certain tissues of patients dead of chorea, especially in the spinal fluid, while some of their pupils were able in experimental animals to develop nervous symptoms analogous to the symptoms of chorea as it exists in the human; and from the brains of such animals the *Diplococcus rheumaticus* was recovered. In spite of this work, however, the medical profession for the most part remained unconvinced that chorea is of proved infectious origin, and it must be said that the chemical findings in the spinal fluid and the cell counts, both in this fluid and in the blood, are not what experience would lead one to expect in a disease of bacterial origin.

Pathologists have nevertheless continued their search for an infec-

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tive factor in this disease, but apparently with little satisfaction. The results of bacteriologic examinations have been most contradictory, whether it has been throat secretions, blood or spinal fluid that has been explored. Negative results have rewarded La Fétra, Bartley, Koplik, Morse, Collins and Passini, although streptococci have grown for Richards, Morse and La Fétra in a small proportion of their cases; staphylococci for Donath, diplococci for Apert, Richter and Collins. All these positive results have been reported in cases uncomplicated by symptoms of rheumatism or endocarditis. In instances in which the disease has accompanied rheumatism, tonsillitis or endocarditis, Richards, Poynton and Camesa have reported positive findings of streptococcus or diplo-streptococcus, while Poynton and Paine have recovered the diplo-streptococcus from rheumatic patients and Rothstein a hemolytic streptococcus from tonsils of choreic patients. Spinal fluids in this disease have been cultured by but few, among these Collins, Passini and Morse and Floyd, all of these with negative results. Animal experimentation has been attempted by Poynton and Paine, Pianese, Donath and Dick and Rothstein. None of these observers have reported results that can be considered conclusive. The latest and most suggestive study is that of Quigley.

Quigley reports that of 21 cases studied 10 yielded positive cultures from both the blood and spinal fluid, and 14 in either one or the other. Six bacterial strains isolated from the tonsil, 8 from the spinal fluid and 9 from the blood, were identical in their morphologic and cultural characteristics. It therefore seems to him that bacteria are of importance in the etiology of chorea, and he believes that the coccus described by him is the organism most frequently present in this disease. He finds this opinion supported, not only by his own work, but after a critical review of the work of others. He thinks that the grouping of the organism, its slow, scant, pin-point growth on blood agar, the slight turbidity and the fine granular sediment which it produces in broth, relate it to the streptococci. In the predominance of pairs, with few short chains, and a few irregular groups, when grown in broth, it resembles the streptococci also, and especially the streptococci or diplococci frequently found in rheumatic fever and in endocarditis. It should be noted that the strains studied do not as a rule cause hemolysis on blood agar plates. No definite grouping can be made on the basis of the fermentative reactions as observed.

So far experiments on animals with this coccus, which is being studied further, have been inconclusive.

Although one may not accept the dictum of Faber that "it is generally recognized that chorea is a bacterial disease due to the *Streptococcus viridans* group" it is difficult to escape the conviction that in many cases, at least, of chorea we are dealing with a general infection with special localization of bacteria or bacterial products in the nervous system. Besides the scanty evidence already quoted, there are a few reports to be found in the literature in which diplococci or streptococci were revealed at necropsy, or in which emboli were found deep in the cortex. However, when one considers that chorea is rarely a fatal disease, necropsy findings on individuals who have died with chorea can not be accepted as conclusively demonstrating the presence of such infective organisms in most cases of chorea. Nevertheless, there is sufficient evidence to justify the physician in an attempt to treat the malady on an assumption of its infectious origin and when the unsatisfactory results that follow the usual methods of treatment are considered, such an attempt seems doubly worth while.

It is the merit of Goodman that he has attempted to apply to the treatment of this disease modern principles of immunity and to introduce immune bodies produced in the patient's blood into the dural space in order that invading organisms shall the more readily be destroyed. His method, briefly, is to remove 45 or 50 c.c. of blood from a vein of the patient, separate the serum and inject this serum into the spinal canal after the withdrawal of a somewhat larger amount of spinal fluid. This injection may be repeated from one to four times. According to his report the results that followed this treatment were amazing. To quote Goodman: "With the autoserum treatment the result is manifest within two or three days—usually one injection is sufficient." Goodman made no differentiation between his mild and severe cases and he classed his results on the basis of the cessation of twitching. In his terminology a "cure" is an absolute disappearance of twitching within a week; "marked improvement," a cessation of twitching within two weeks; "slight improvement" when the movements disappear by the end of the third week; and if after four weeks there is still involuntary movement, he classes the case as "unimproved." Of course, in estimating the cure of chorea much else should be noted besides the twitching. The emotional state of the patient, his fatigueability and the reinstatement of his cerebral inhibition over voluntary movement are of equal if not of greater importance in gaging progress toward returning health.

I was attracted to the Goodman treatment through an opportunity given me by Dr. H. K. Faber to watch the course of events after treatment given one of the patients at the Stanford University Hospital. Faber treated three cases by this method and reported them. He was very much impressed with the results, as in each instance almost complete cessation of the symptoms followed within a week after a single injection of autogenous serum.

In considering the results attained by Goodman's treatment it occurred to me that perhaps the whole effect was attained because the injection of the autogenous serum had set up a sterile meningitis and so had increased the permeability of the choroid to such a degree that antibodies were able to pass from the blood stream into the lymph spaces of the central nervous system. It is well recognized, due to the published work of Mott, Leri, Orofici, Flexner and Mehrtens, supported by other unpublished work, that the injection of foreign protein does break down the defensive power of the choroid and allow substances which ordinarily do not pass to move from the blood into the central nervous system. Goodman, himself, insists that it is necessary to withhold all medication for some days before instituting the treatment. One of his patients who had been receiving chloral and codein, went into deep coma which lasted for thirty-six hours after the first injection. This circumstance was attributed to "some chemical action in the blood plasma which causes a very potent action of drugs when injected into the spinal canal." There is reason to believe, however, that this result was due to an increased choroidal permeability produced by the proteins injected into the spinal canal. This possibility is most clearly set forth in the researches of Flexner and Amoss, who, working on poliomyelitis, first showed that antibodies might be drawn from the blood into the spinal fluid following the introduction of irritants into the subarachnoid space. They were able to grade these irritants in order of their potency from horse serum, which was the most powerful, down to simple drainage of the cerebrospinal canal, which was least irritating. Ranging between these two extremes were the power of heterologous serums, homologous serums, and hypotonic and hypertonic salt solution. Mehrtens has demonstrated that homologous serum injected into the subarachnoid space produces an irritation manifested by a cell count sometimes as high as 1,800 cells to the cubic millimeter, and that a drainage of 30 to 50 c.c. of spinal fluid may be followed by the secretion of a fluid containing as high as 10 to 80 cells. Mehrtens was able to bring sodium iodid out of the blood into the spinal fluid by injecting the drug intravenously six hours after an injection of 10 c.c. of normal horse serum had been made into the subarachnoid space.

These facts, taken together with the knowledge that horse serum injected in the form of immune antimeningococcus serum is innocuous to children, seemed to warrant the use of horse serum by intrathecal injections in the treatment of some cases of chorea admitted to the Hospital for Children in San Francisco. Seven patients have received such injections, and another case has been treated by the method Mehrtens of Stanford University is using in the treatment of cerebrospinal syphilis, namely, the injection of salvarsan six to twelve hours after the preliminary intrathecal injection of horse serum. Of the cases so treated, one was of the maniacal type, quite the most severe case conceivable; one was of severe hemichorea with pseudoparesis; two very severe; one was of moderate severity, and two were mild, although one of these had been very persistent; three of the attacks were recurrences. The first four patients treated received an initial injection of 20 c.c. of normal inactivated horse serum half an hour after a half c.c. of the same serum had been given subcutaneously in order to test whether or not the patient was hypersensitive to the serum. Five of the patients received a second injection on the fourth, fifth and sixth day following the initial treatment. One little girl reacted so violently to the first injection that repetition was deemed inadvisable, and through a mistake another was allowed to go beyond the period of anaphylactic sensitization, so in this case also it was thought best to forego the second injection. Two patients received injections of 10 c.c. only.

Accepting the premise that the mechanism behind Goodman's results was a protein reaction which let down the choroid plexus barrier that prevents circulating antibodies from entering the spinal fluid, it is obviously of advantage to use normal horse serum instead of autogenous, because the former is more convenient to obtain and to administer and at the same time it is a more potent irritant to the meningeal structures than is homologous serum.

Two sets of unpleasant reactions have followed the use of the horse serum within the spinal canal, an immediate reaction which was evidenced by prostration, by headache, and sometimes by severe vomiting. These phenomena also appear after the injection of homologous serum. They are familiar to those therapists who use the Swift-Ellis technic in the treatment of syphilis. Goodman attributes these untoward symptoms to pressure, but, as in his cases and in this series, uniformly an amount of serum was injected less than that of the spinal fluid withdrawn, pressure cannot be incriminated. The knowledge Flexner and Amoss gained for us about the irritating quality of serum injections is confirmed by the cell counts made by Mehrtens ten hours after the injection of horse serum, when that observer showed a pleocytosis of from 10,000 to 80,000 cells to the cubic millimeter. Further confirmation was had by our own cell counts and the results of chemical reactions in fluids withdrawn from eight to fourteen hours after the injections. It is striking that the only child who showed no improvement after these injections was one whose spinal meninges did not react to the serum by an increased cell count. The second unpleasant reaction appeared after a week and was evidenced by the usual symptom of serum disease; the distressing urticaria was readily counteracted by injections of epinephrin given subcutaneously.

The number of cases treated is too few from which to draw valid conclusions; however, if we use Goodman's criteria, the injections of horse serum have been instrumental in gaining striking and rapid improvement in most cases, but no improvement has been such that a cure can be claimed on the basis of "absolute cessation of all twitching within a week." In fact, only in the mild cases was twitching entirely absent after two weeks, and all three of these patients had been affected for at least three weeks before treatment was inaugurated. One patient, a girl (a mental defective with a neurotic heredity), showed absolutely no reaction to the injections of serum. The most striking results followed the use of the horse serum in the maniacal and very severe cases. Before the serum was used, two of these patients could be kept in bed only by the use of restraining packs, but within forty-eight hours after the first injections both were able to carry a cup to their mouths and to drink without any assistance from the nurse. The restraining pack was no longer necessary and there was a steady diminution in all the excessive movements, while the mental conditions, especially the emotional overflow, were markedly improved. By the end of the third week it was with difficulty that choreic movements could be brought out, but even then they could be elicited by allowing excessive excitement or persistent mental strain to affect the patient.

Undoubtedly the use of horse serum is of great value in controlling these very severe cases. My experience with the Goodman treatment is not sufficient to allow me to express a personal opinion; but, accepting his findings, it seems that the autogenous serum is a therapeutic agent preferable to horse serum in chorea. One would not choose to use horse serum in the treatment of any moderately severe or mild case, but in any attack of great severity the method will certainly bring rapid benefit to the patient.

The last child treated received 5 c.c. of horse serum in the spinal canal, and this was followed in twelve hours by half the normal adult dose of arsphenamin by the vein. The case was an exceedingly severe one, especially on the emotional side, and while there seemed to be marked amelioration, immediately after the treatment, which persisted for some weeks, there has since been retrogression. It is, of course, impossible to draw conclusions from a single case treated so recently, but on the whole the result obtained does not encourage the hope that this is any advance on other methods of treatment.

We have been struck by the fact that injections of smaller amounts of the serum are as effective as are the larger. In future, in applying this technic, not more than 5 or 10 c.c. of serum will be used at a single injection. The value of repeated injections also seems to be demonstrated. The headache and depression that followed the first injection are rarely manifest after subsequent treatments.

The fact that the withdrawal of blood from a donor and the preparation of a sterile homologous serum present great technical difficulties, while sterile normal horse serum is easily obtainable and the technic of its use is simple, led to the hope that the use of the latter agent might give the profession a valuable means of dealing with a distressing malady. A measure that could be applied without harm to patients outside the protecting walls of a hospital. The cases here reported are too few to say that the hope is realized, but there can be no doubt that in the most severe cases the injections of normal horse serum bring about rapid diminution of the more explosive symptoms. Parents who naturally are uneasy during the stage of first reaction following a treatment are uniformly delighted at the promptness with which their children gain control of movement and speech and lose their emotional excitability.

Of course, this method is no panacea for chorea. The fact that these children have a congenital inferiority of the nervous system means that rest and overfeeding will always be essential parts of the treatment. Head's dictum that the cure for chorea is six weeks in bed, four eggs and two quarts of milk a day, must still be remembered; nor must it be forgotten that any focus of infection, especially if it be in the tonsil, must be removed. Warm baths and massage ought never be omitted from the regimen. Care must also be taken to heed the psychologic reaction inevitable between choreic patients and their environment. Therefore, it is wise to keep the family and the usual attendants away from close contact with such children during the course of treatment. Under such management mild cases of chorea will rapidly achieve normality. However, when the patient is affected with severer forms the results of such measures are delayed for weeks or months. In these circumstances the little patients become a great distress to themselves and to all about them, and it is to such that the intrathecal injections of horse serum offer a therapeutic aid which is harmless and which at the same time will bring prompt relief to the more dominant symptoms, and probably, though not certainly, will hasten the final recovery.

While there is no certainty that chorea is an infectious disease, treatment based on that idea can be warranted only by clinical results. Never can the psychic disturbance of chorea be overlooked, and it may well be that the results which follow the use of serums are evidence of a successful, if unwitting, application of suggestive therapy. At any rate we have every right to hope that further investigation will establish the serums as valuable measures in the treatment of selected cases of chorea.

SUMMARY OF CASES

Case 1.—O. W., boy, aged 11 years; second attack; duration two weeks from commencement of treatment; very severe maniacal delusions and great excitability; had to be restrained in bed; characteristic twitchings; unable to speak intelligibly; heart normal; tonsils showed chronic infection. Injection of 20 c.c. of serum given, followed by vomiting, prostration, slight pyrexia, and immediate exaggeration of all symptoms; reaction disappeared in thirty-six hours. Second injection of 20 c.c. was given on the fifth day following. All twitching had disappeared in forty-eight hours. The excitability with emotional overflow persisted for about two weeks. Besides the serum treatment, the patient had continuous hot packs. a high calory diet, and during the third week in the hospital, tonsillectomy. There was a relapse during the two weeks following the removal of the tonsils. During the next two weeks all symptoms disappeared. The patient was dismissed and has remained free for two months.

Case 2.—M. P., girl, aged 8 years. The patient, who had a neurotic family history and was a masturbator and a mental defective, had had a persistent chorea with short periods of remission for the previous three years, although the manifestations were mild. Her symptoms were twitching, emotional excitability and overflow, a clumsy gait and blurred speech. Her heart was normal; throat was healthy. She was given 20 c.c. of serum on two occasions, four days apart. A slight reaction, with vomiting, headache and low fever, persisted for forty-eight hours after the first injection. She had slight diminution of symptoms after the second day, but final result showed her to be no better than before treatment. This is the only case in which some definite influence over the course of the disease was not manifest.

Case 3.—J. H., girl, aged 11 years; second attack; was very severe. There were many other cases of chorea recorded in the family history. She had been ill for eight weeks. Her symptoms were twitching, persistent headache, speech disturbance, excitability, emotional overflow. She had chronic inflamed tonsils and had suffered from recurrent tonsillitis. She received 20 c.c. of serum without a second injection and she reacted to the serum with headaches, stiff neck, stiff legs, vomiting and later a severe urticaria, all of which symptoms disappeared within forty-eight hours. Improvement began at this time and continued uninterruptedly. She was dismissed after three weeks perfectly well. Besides the serum she received a high calory diet and a short course of hot packs.

Case 4.—L. S., boy, aged 13 years; severe attack, hemichorea type, which was the second attack. He had suffered from a very severe seizure two years before. The duration of the present attack was three weeks. Symptoms were twitching, right pseudoparesis, emotional disturbance, speech disability. He was hardly able to walk. The heart showed a slight systolic blow; no endocarditis. He had chronic recurrent tonsillitis. Received 10 c.c. of serum and no second injection. He reacted with headache, slight urticaria and slight purpura, all of which disappeared in thirty-six hours. He showed a steady improvement and had a slight relapse lasting for about three days after the removal of his tonsils during the second week of treatment. He was dismissed in a month, having showed no further symptoms after the third week. There had been no return of symptoms up to the fourth month.

Case 5.—D. J., girl, aged 13 years. This was a very severe attack, with frequent exacerbations. The patient was so uncontrolled that she had to be restrained in bed. This was the first actual attack, although she had been "very nervous" for the past five months. The actual attack was of three weeks' duration. The symptoms were twitching, loss of motive power, loss of intelligible speech, emotional overflow and a mild adiadokokinesis. Her heart was normal. Her tonsils were slightly injected. She was given an initial dose of 20 c.c. serum and five days later another 20 c.c. She had a violent reaction to the first injection with extreme vomiting and some pyrexia, which persisted for thirty-six hours. A week later there was marked urticaria for one day which was well controlled by epinephrin subcutaneously. The alleviation in this case was striking. The child, who was utterly helpless before treatment, was able within forty-eight hours to feed herself and to drink water from a cup unaided. She went on to complete recovery and was dismissed without symptoms at the end of her third week in the hospital. She was given high calory diet, hot packs, as well as serum treatment. A cure could not be claimed, because she was still highly emotional, and she had a short relapse two months after leaving the hospital.

Case 6.—V. B., girl, aged 10 years. First attack, but "always nervous." The duration of the attack was three weeks. It was a mild case, evidenced by twitching, emotional overflow and slight speech disturbance. Her heart was normal. She had chronic recurrent tonsillitis. The first injection was 7 c.c. of serum and the second 10 c.c. The reaction was slight and she complained of a mild headache and backache. She had low fever and was restless. The symptoms of chorea were exaggerated for the first two days; then there was steady improvement. Her tonsils were removed two days before the serum was injected. She was given high calory diet. Her progress was uninterrupted and the symptoms had disappeared entirely in three weeks.

Case 7.—R. M., boy aged 14 years. Family history not neurotic. This was the fourth attack. The boy had suffered from an attack of rheumatism in his eighth year, and this was followed by chronic endocarditis, and a pseudoparetic chorea, lasting four months. There was a third attack following this, which lasted for six weeks. There was a second attack which lasted six months. His tonsils had been removed between the second and the third attacks. The present seizure had lasted two weeks. He had lost power to use his right hand, he dragged his right leg, his speech was greatly disturbed, he had marked choreic movements and emotional overflow. His heart showed the evidence of old endocarditis; his throat was healthy, tonsils out. He received an initial injection of 20 c.c. of serum and a second dose four days later of another 20 c.c. After the first injection he reacted with headache, vomiting, anorexia and the choreic symptoms were worse. Within forty-eight hours this reaction abated and from that time he made a rapid improvement. Packs and high calory diet were also prescribed. The symptoms were entirely gone in two weeks and he had no return after six months.

BREATH HOLDING IN INFANTS *

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Breath holding (also known as hysterical laryngospasm, rage spasm, and inspiratory apnea) is a condition not infrequently observed in early childhood. At first glance one would be led to believe that the attacks are manifestations of spasmophilia or tetany with the associated laryngismus stridulus, but on closer investigation it will be discovered that such assumptions are erroneous. The breath holding attacks, as distinguished from laryngismus stridulus, manifest no true laryngeal spasm. The breathing stops suddenly in the midst of a crying attack, but there is no inspiratory spasm.

The attack may be briefly described as follows: The child works himself into a rage, cries for a time, and then suddenly stops, finding it impossible, for a brief period, to make any further sound. The inspiratory muscles remain in a tonic state. The child throws himself about and becomes cyanotic or pale. Then the body becomes rigid and the eyes turn or become set. For a moment it seems that the child is asphyxiated. The attack usually lasts a few seconds and then disappears. It may, however, continue for several minutes, while in the more severe cases it may be followed by convulsions.

Barthez and Rilliet are among the first to speak of breath holding. They describe it as a condition occurring in passionate (angered) children, manifested by a suspension of the respiration accompanied by suffocating inspiration, during which the face becomes purplish and the extremeties cold. Sometimes it is followed by an eclamptic attack. They say it is not possible to distinguish breath holding from glottis spasm.

Ibrahim reports three cases, the first two of which are dismissed with only a short reference. In the first there had been laryngismus stridulus of the ordinary type in early infancy. In both, the rage spasms were characterized by emotional excitation, cyanosis, unconsciousness, and great drowsiness. The third case is described in great detail, the principal points of which were the following: The mother was an extremely nervous woman and is said herself to have suffered from rage spasm during infancy. The infant thus had a nervous stigma, although there was neither epilepsy, insanity, nor other ner-

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* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

vous disease in the family history. Ibrahim had this baby under observation since earliest infancy. During the second year, the child in the midst of a crying attack would hold its breath and become cyanotic; the body would grow limp. Respiration would apparently cease. At the end of the attack, the child would cry lustily for a few moments and soon afterward fall asleep.

Ibrahim calls attention to the fact that all the classical signs of tetany, including the electrical reactions, were searched for but were not found.

H. Neumann[1] in his discussion of breath holding, tries to differentiate it from tetany. Laryngismus stridulus, he says, is a manifestation of spasmophilic diathesis or tetany and tends to disappear during the first year or two of life; whereas the inspiratory apnea or breath holding attack is an early symptom of neurasthenia. He also says that in numerous cases which he has examined, the classical signs of tetany were usually absent. There was one exception, however, a boy of 4 years, who, suffering evidently from rage spasm, showed very definitely Chvostek's facial phenomenon. His father, who was an extremely neuropathic individual, showed the same sign.

A further differentiation may be made in addition to Neumann's observations. Attacks of breath holding occur commonly in the second and third years of life and tend to disappear about the fifth; whereas genuine spasmophilia makes its appearance during the first year or two.

It will occur to everyone that the resemblance between these breath holding attacks and minor epilepsy is such that the differentiation of the two may at times present great difficulties. It should be remembered, however, that breath holding attacks follow immediately after severe crying, excitement, or anger; while epileptic attacks occur suddenly in the midst of quiet play or even during sleep. Biting of the tongue, which is characteristic of epilepsy, does not occur in breath holding. On the other hand, involuntary evacuation of the bladder or rectum may occur in either attack. Another point of resemblance is the prolonged sleep usually following an attack which is characteristic of both conditions.

Neumann reports a case in which breath holding attacks or rage spasm occurred in an epileptic child 3 years old. He had suffered from epilepsy since his third month of life and presented at times unmistakable convulsive seizures. On certain occasions, however, when he lost his temper or became frightened, he would hold his breath, become cyanotic, and after a brief period would lapse into a deep sleep.

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* Arch. f. Kinderh., **42.**

It would seem that an important point in the differentiation of the two conditions is to be noted in each case in the progress of the disease, namely, that breath holding attacks tend to recover completely, while epilepsy, as a rule, persists.

I have seen on several occasions attacks of whooping cough in young infants and children that required differentiation from breath holding seizures. A few days ago, for instance, a child was brought into my office because of peculiar respiratory attacks that alternated with coughing. At night the child not infrequently had severe coughing attacks which the parents thought resembled whooping cough. During the day, however, the coughing was substituted by paroxysms of breath holding; undoubtedly they were voluntary attempts to suppress the cough. They were characterized by extreme cyanosis, great prostration, relaxation of muscles and momentary unconsciousness. The baby gives one or two short coughs, then she becomes blue and rigid. She has a facial spasm, the eyes become set and roll upward, arms and legs are rigid and the mouth is tightly closed. The attack lasts several minutes. Cyanosis disappears, normal breathing is resumed and consciousness returns. This seventeen months old baby had such an attack in my office. These alternating attacks of coughing and breath holding had been going on for four or five weeks, during which time one or more typical whooping cough paroxysms occurred almost nightly.

I also recall the history of a baby 2 weeks old who acquired whooping cough from the mother. The child began to cough when it was only 10 days old. Each paroxysm was characterized by a slight crowing. He would become intensely cyanotic and fall limp in the mother's arms with complete respiratory cessation. At such times, the pulse was slow and the child seemed lifeless. After a few moments the patient regained color, and breathing proceeded normally. The baby ultimately recovered.

Cases of breath holding are not of uncommon occurrence. Very often they are the cause for emergency calls for the medical attendant, though as a rule, he discovers when he arrives on the scene that the child has recovered. Only the other day a mother came to my dispensary clinic with a large, well developed baby of 22 months, who presented all the characteristics of breath holding or rage spasm. The mother described in minutest detail all of the points which have already been referred to. If the child was crossed or thwarted in any way, it would cry, hold its breath, become cyanosed and momentarily unconscious. The child was very well nourished, presented no evidence of rickets, no carpopedal spasm, and no Chvostek or Trousseau signs.

Another case further illustrates the disorder. A mother brought her 17 months old baby to us on May 5, 1918, because of anemia and great fretfulness. The child had always been delicate and sickly, was very difficult to feed, and suffered from severe malnutrition. She was extremely irritable and cried much of the time. About two weeks before we saw her the child began to fret more than usual, would become extremely irritable and work herself into a rage, which would be followed by a breath holding spasm. The mother said that five or six of these attacks occurred daily. None of the typical signs of tetany was present, though there was a slight increase of electrical excitability. We improved the child's feeding and suggested a plan of psychotherapeutic treatment which the mother, who was a very intelligent woman, immediately adopted. She refused to pick up the child when she cried, treated her sternly, shook her finger at her, and reproved her when a breath holding attack was imminent or in progress. The treatment finally proved successful. Although on the first day after the baby's admission to the hospital we were enabled to witness several typical attacks which consisted of fits of temper, crying, breath holding, cyanosis and momentary unconsciousness, on the second day they had completely ceased.

These attacks of breath holding occur in neuropathic children and are brought on by fear, anger, fright, or some other psychic trauma. As a rule, children subject to such seizures are irritable and ill-tempered. The condition is very often aggravated by neuropathic parents who, fearing the recurrences of these attacks, humor them in every possible way, permitting no one to cross the child and allowing no whim or caprice to remain ungratified. It is obvious, of course, that such treatment does not help the child to build up any degree of resistance to the recurring attacks.

After some time has elapsed, most of these patients practically recover, although in some instances, as has been pointed out, the attacks may be severe and protracted. Children who fall ill with an acute infectious disease, or who, by reason of accident or injury, require surgical treatment, may be seized with a severe breath holding attack, accompanied by general convulsions, as a result of the fright which they have sustained. Under such circumstances the attack may be so severe as to terminate fatally.

Treatment should be directed toward the general management of the nervous child. Mental stimulation of every kind should be avoided. He should be ignored as much as possible by parents and friends. When the attacks occur, there should be no fussiness or consternation, or any of the hysterical manifestations usually evinced by mother or nurse. Cold water dashed into the face has been suggested as a direct remedy. Finally, the patient should be shown in no uncertain manner that any repetition of the attack will meet with harsh if not painful measures.

Frequently the patients improve most rapidly when they are removed from the excitement and tension of home surroundings. A short stay at the hospital away from parents and friends is often advisable. At times a short course of bromids may be required in addition to psychotherapy.

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BALANTIDIUM COLI INFECTION WITH REPORT OF A CASE IN A CHILD *

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NEW ORLEANS

There appeared in my service in the outpatient department of the Touro Infirmary in New Orleans an interesting and unusual case of dysentery which because of the age of the patient, the source of the infection and the character of the organism found deserves recording if for no other reason than as a reminder of another possible etiologic factor in the production of frequent stools. The infrequency of many diseases in childhood undoubtedly is in great part due to lessened exposure incident to age. This explanation advanced several years ago in the instance of amebiasis in children may also be suggested for the rare infection in childhood of this unusual offender in man.

While the case was not observed for as long a time as would have been preferred, nevertheless for the foregoing reasons and because of the easy means of its recognition, this case of *Balantidium coli* in a child is reported.

REPORT OF CASE

History.—A colored boy 5 years of age was brought to the outpatient children's department at Touro Infirmary by his mother who stated that the child had been having a diarrhea for nearly a year, but that recently she noticed blood in his bowel movements. During the period from the first attack of diarrhea to the present time there had been intervals when the child was apparently well and had no bowel trouble. With this last attack, however, blood had appeared and he seemed sicker than ever. The attacks were progressive in severity, each one being worse than the one preceding. He strained when his bowels moved, complained of pain in his stomach, had no appetite, and had been losing weight. He had been accustomed to help "round up" the pigs in the pen every day and frequently would eat some food which he would hold in his hand while helping with the pigs. It was his habit also to go into the pen at times when he ate his food.

The family history was negative, except that the father, who tended the pigs, had a diarrhea a short time previously, the character of which could not be ascertained.

Past History.—The patient was a full term child. He had never been ill before the diarrhea, and had always been nourished as other children of his race.

Physical Examination.—This showed a patient poorly nourished but fairly well developed. His skin was dry, as was his tongue and mouth. There was a catarrhal stomatitis. His eyes were sunken. His lungs, heart, liver, spleen and abdomen were negative except for some tenderness over the lower abdomen. The nervous system was also negative.

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A rectal tube was passed and some bloody mucus obtained, which was immediately examined and revealed the presence of *Balantidium coli.*

As there were no beds available at Touro Infirmary he was referred to my service at the Charity Hospital, but unfortunately he never appeared at the hospital and was lost sight of.

Description of Organism.—The organisms seen in this case belonged to the infusoria variety of the protozoa and are known as *Balantidium coli.* They were oval-shaped, more pointed and tapering at one end and rounded at the other, and measured from 0.07 to 0.1 mm. in length by 0.05 to 0.07 mm. in breadth. The mouth was funnel-shaped and situated on the ventral side of the organism a little below the anterior or pointed pole. A thick layer of long cilia was found around the peristome, which continued actively a circulatory motion, and by the use of which the organism grasped its food: various cells, bacteria, and blood cells. The funnel-shaped mouth extended backward and downward and communicated with the endosarc.

The endosarc consisted of granular matter both fine and coarse and highly refractile, inclosed in a thin and very transparent sheath, which was a continuation of the gullet above and which ended at the anus situated at the posterior or more rounded pole. A kidney-shaped nucleus, which changed its position with the motion of the granular matter, was found in the endosarc usually below and to one side of the peristome. Vacuoles were seen in the endosarc numbering from one to six, usually two, and were apparently contractile. These vacuoles according to Stein[1] are connected by lacunae, which probably explains the large single vacuole sometimes seen which occupies the whole lower third of the parasite.

A thick cuticle longitudinally striated inclosed the endosarc and was separated from it by a narrow rim of homogeneous protoplasm (the ectosarc). These striations, undoubtedly muscular structures, extended from the peristome on the ventral surface and from a corresponding level on the dorsal surface to the anus of the posterior pole.

Cilia extending throughout the entire length of these striations controlled the movements of the parasite.

By means of these cilia and muscular bands the parasite was able to move with tremendous rapidity and comparative ease through fields containing large particles of matter. The parasite was capable of changing its shape and direction with great facility by contracting the muscular bands.

At times the organisms appeared quite round.

Encysted forms of the parasite have been described by Leuckart[2] and Stein,[1] in which the organism becomes rounded, loses its cilia, the endosarc contracts and contains fat globules, the nucleus becomes obscured, and it is surrounded by a thick capsule.

From the careful observations of Bel and Couret[3] through the entire cycle the method of reproduction of these infusoria is by budding conjugation and binary fission. Many other methods of conjugation and reproduction have been described by Wising,[4] Woit,[5]

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[1] Stein, F.: Bohmisch. Genzell der Wissenchaften, 1860, p. 165; Amtl. Ber. d. Karlsbad, Naturforch., 1862.

[2] Leuckart: Die menschlichen Parasiten, 1863, p. 1; Parasiten des Menschen, 1879, p. 3.

[3] Bel and Couret: Balantidium Coli Infection in Man, Jour. Infect. Dis., 1910, **7,** 609.

[4] Wising, P. J.: Nord. med. Arch., 1871, **3,** No. 3, Stockholm; Ibid., Svensk. Läk. Sällsk. Handl., 1885, p. 48, Stockholm.

[5] Woit, O.: Deutsch. Arch. f. klin. Med., 1897, **60,** 363.

Gurvich,[6] Bushuyeff,[7] Lavrovskaya,[8] Zhegaloff[9] and Daflein.[10] The observations of Bel and Couret[3] with regard to reproduction conform to those of Ekecrantz,[11] Wising,[4] Leuckart,[2] Strong[12] and others.

Conflicting results have been obtained from animal experimentation by Wising,[4] Lavrovskaya,[8] Strong,[12] Zhegaloff,[9] Rapchevski,[13] Chigayeff,[14] Vlayeff,[15] Cassagrandi and Barbagello[16] and Chichulin[17] by injecting feces containing balantidia in cats, dogs, rabbits, pigs and monkeys.

Grassi and Calandruccio[18] produced no results on themselves after injecting balantidia from the hog.

Leuckart[19] describes these organisms as being much less sensible to the influence of water and cold than other nomads, and as preserving their viability and motility for long periods in water at ordinary temperature. Klein[20] recognized an organism which he believed to be *Balantidium coli* which he secured from sewage and which after being bottled in sewage lived and were yet motile in thirteen weeks. On the other hand, Malmsten[21] concluded that the parasite is short lived, since it died shortly after removal from the intestine, and Zhegaloff[9] was of the same opinion. From the various statements made by observers it may be said that the length of time the organism may live is variable. Attempts to prolong their lives in feces by Bel and Couret[3] were unsuccessful at various temperatures, as were also their attempts at the cultivation of the organism. Other observers have met with the same negative results, and Strong[12] states that the parasite has not been grown or isolated in pure cultures.

Balantidium coli were probably first observed by Lieuwenholk[22] in his own stools in 1857. In 1857 Malmsten and Loven[23] first described them as *Paramecium coli,* and five years later (1862) Malmsten[24] reported two cases. Stein,[1] in 1862, proposed the name of *Balantidium coli.*

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[6] Gurvich, M. J.: Russk. Arch. Patol., I. Bakteriol., 1896, **2,** 804.

[7] Bushuyeff, V. F.: Voyenno-medic. Jour., 1897, p. 188, Med. Spec. Part, p. 167.

[8] Lavrovskaya, Y.: Bolnitch Gaz. Botkina, 1891, No. 11, p. 304, St. Petersburg.

[9] Zhegaloff, J. P.: Klin. Jour. Mosk., 1899, **1,** 44.

[10] Doflein, F.: Die Protozen als Parasit. u. Krankheitserreger, Jena, 1901.

[11] Ekecrantz, W.: Nord. Med. Arch., 1869, p. 1, Stockholm.

[12] Strong, R. P.: Dept. of Interior, Bureau of Govt. Lab. Biol. Survey, No. 26, December, 1904.

[13] Rapchevski, I. F.: Vratch, St. Petersburg, 1880, p. 505; Med. Vestulk, St. Petersburg, 1882, **21,** 361, 377 and 393.

[14] Chigayeff, N. F.: Vratch, St. Petersburg, 1898, **19,** 1441.

[15] Vlayeff: Vratch, St. Petersburg, 1898, **19,** 140.

[16] Cassagrandi and Barbagello (Quoted by Strong, Footnote 12).

[17] Chichulin, G. N.: Voyenno Med., 1900, **78,** Med. Spec. Part, p. 3059, St. Petersburg.

[18] Grassi and Calandruccio: Acc. d. R. Acad. d. Linc., Roma, 1888, 285, series 4, vol. 4, p. 700.

[19] Leuckart: Brit. Med. Jour., Dec. 19, 1896, p. 1797.

[20] Klein, E.: Brit. Med. Jour., 1896, **2,** p. 1852.

[21] Malmsten, P. H.: Allg. med. Centr. Ztg., Berl., 1858, **27,** 81.

[22] Lieuwenholk: Quoted by Strong, Bull. Johns Hopkins Hosp., 1901, **12,** 31.

In 1891 Mitter[25] was able to collect only twenty-eight cases. Strong,[12] in 1901, only 117 cases, including reports from Africa, Cochin China, Cuba, Finland, Germany, Italy, North and South America, Philippines, Russia, Sunda Islands and Sweden.

In the United States probably the first case to be reported was in Iowa by Mitter[25] in 1891. Since then cases have been reported by Bel and Couret,[3] 1 in Louisiana; Gray,[26] 3 in Arkansas; Deaderick,[27] 1 in Eastern Arkansas; Sistrunk,[28] 1 in Minnesota; Rockefeller Sanitary Commission,[29] 2 in North Carolina and 1 in Mississippi; Jennings,[30] 1 in New York; Bowman,[31] 2 in the Philippine Islands; and Young and Walker,[32] 1 case in Oklahoma.

In all, the literature contains considerably less than 150 reported cases of this infection in man. Men have been infected twice as frequently as women, and in the cases reported all have been adults with the exception of two cases in children.

The habitat of this infusorium in the human being is in the large intestine, but they have been found in the appendix (Malmsten[21]).

Leuckart[33] was the first to show the pig to be the normal host of the *Balantidium coli.* He suggested that the possible way infection occurred was by the entrance of the freshly voided parasites into the alimentary tract of the human being. He also suggested ingestion of the organism in the encysted state as a probable method of infection.

Deaderick[27] says that besides the domestic pig, certain species of monkeys serve as hosts for the balantidium.

The observation of Klein,[20] who found an organism he believed to be the *Balantidium coli* in the sewage of London, and also in the drinking water of the same city as delivered to the consumer, suggests the entrance of the organism through drinking water as a means of infection.

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[23] Malmsten, P. H., and Loven: Infusurier säsom intestinaljar homemeskan, Hygeia, Stockholm, 1857, **19,** 491; Virchows Arch. f. path. Anat., 1857, **12,** 302.

[24] Malmsten, P. H.: Quoted by Strong and Musgrove, Bull. Johns Hopkins Hosp., 1901, **12,** 31.

[25] Mitter, J. J.: Beitrag z. Kenntness zur Balantidium Coli in Menschlichen Darmkanale, Kiel, 1891.

[26] Gray, D. A.: St. Louis Med. Rev., April 27, 1907.

[27] Deaderick: Endemic Diseases of Southern States, 1916.

[28] Sistrunk, W. E.: Intestinal Parasites Found in Individuals Residing in the Northwest, Jour. Am. Med. Assn., 1911, **57,** 1507.

[29] Rockefeller Sanitary Commission Reports, 1911, 1912 and 1913.

[30] Jennings: New York State Jour. Med., 1912, **12,** 179.

[31] Bowman, F. S.: Studies in Balantidium Infection, Med. Rec., New York, April 22, 1911.

[32] Young, A. O., and Walker, O. J.: Balantidium Coli Infection in Oklahoma, Jour. Am. Med. Assn., 1918, **70,** 507.

[33] Leuckart: Weighman's Arch., 1861, **1,** 80, Plate V, Fig. A, B; Die menschlichen Parasiten, 1863, p. 146; Fig. 21, p. 744.

It is of interest to note that in about 25 per cent. of the cases reported infected with *Balantidium coli* there has been either direct contact with swine or the infection has followed ingestion of food products from pork.

An entire family infected with *Balantidium coli* after eating sausages made from a hog which had harbored the organism is reported by Chichulin.[34]

Henschen[35] especially emphasizes the pathologic importance of the parasite, while other authors are inclined to believe the presence of the parasite to be an accidental or unimportant complication.

In 1900 Opie,[36] in his article on protozoa, concludes "that *Balantidium coli* is apparently an accidental parasite which finds favorable conditions for growth in the diseased intestine, and that it is improbable that the organism is the etiologic factor in the production of the diarrhea with which it is associated."

McFarland[37] holds that the organism is not certainly parasitic, but perhaps merely commensal; that is, it inhabits the body of its host, but without any effect on the host either detrimental or advantageous.

Malmsten[21] and Doflein[10] believe the organism to be harmless, but Strong,[12] Brooks,[38] Solowjew,[39] Bel and Couret[3] and others believe the balantidium is an important etiologic factor in the production of the catarrhal and ulcerative lesions of the large intestine in the infection associated with its presence.

Certainly the cases of Strong and Musgrave[40] and Bel and Couret,[3] which have been so carefully and minutely studied, are conclusive evidence of the pathogenicity of the organism. To quote their conclusions:

> Strong and Musgrave:[42] We cannot regard this parasite as a harmless one for we could not explain the persistent diarrhea of our patient without regarding it as the exciting cause, nor were we from the lesions found at necropsy enabled to explain his death in any other way.
>
> Bel and Couret:[3] Finally, from the definite and constant microscopic findings and negative blood and cultural results for other intestinal invaders, the logical conclusion seems to be that *Balantidium coli* is not a harmless commensal, as some suppose, but an organism able to invade the human tissues and cause a serious disease; death may follow through compression of the intestinal glands by a hyperplasia of interglandular tissue produced by the parasites and through glandular necrosis and absorption of toxins from any terminal bacterial invasion.

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[34] Chichulin, G. N.: Loc. cit., Footnote 17.

[35] Henschen: Quoted by Strong and Musgrave, Footnote 42.

[36] Opie: Twentieth Century Practice of Medicine, 1900, **19.**

[37] McFarland: Quoted by Jennings, Footnote 30.

[38] Brooks, H.: New York Univ. Bull. Med. Sc., January, 1902.

[39] Solowjew, N.: Centralbl. f. Bact., Ref., 1901, **29,** 821 and 849.

[40] Strong and Musgrave: Bull. Johns Hopkins Hosp., 1901, **12.** 32.

The infectious character of the *Balantidium coli* is seen in the observations of Brooks[40] on a fatal dysentery among the apes in the New York Zoological Garden, and the pathology of the infection in man is clearly shown by the necropsies and studies of Strong and Musgrave,[42] Solowjew,[41] and Bel and Couret.[3]

The organisms invade all the coats and blood vessels and lymph channels of the large intestine and the neighboring lymph glands, and produce a hyperplasia and cell infiltration either mechanically or through the liberation of cytolytic ferments. Ulcers which are small and shallow and mostly limited to the mucosa are found which are probably due to the terminal invading bacteria, the balantidium coli primarily producing avenues of entrance, as they are absent from the walls of the ulcers; some, however, penetrate the muscularis mucosa. The organisms produce a subacute or chronic inflammation of the interglandular tissues and submucosa.

The presence of the organisms in the blood vessels and lymph channels argues for the possibility of carrying infection to the liver and lung through these routes (Couret and Bel[3]).

The patients suffering with this infection may have digestive troubles, but usually have a diarrhea or dysentery. The stools are liquid and may contain undigested food. There is usually mucus or blood, the stools resembling those seen in amebic dysentery. These may be from a few to many in the course of the twenty-four hours. Tormina and tenesmus are frequent, the latter particularly if the lesions are situated near the anus.

The symptoms may subside for a period, to begin again. In those cases of prolonged duration anemia may be found and there is great loss of weight. At times there is edema. In some cases severe and pernicious anemia has been suspected. The course of the disease is usually progressive.

Examination of the blood usually shows slight variations from the normal and there may or may not be an eosinophilia.

The skin is dry, the temperature is normal or there may be a rise up to 99 F. Hebetude is present to a greater or lesser degree, the tongue is dry, at times a stomatitis may be present. The lymph nodes are occasionally enlarged. Emaciation is a common symptom.

The urine shows nothing of interest.

Proctoscopic examination usually reveals the rectum and lower colon lined with thick, bloody mucus covering the shallow ulcers which readily bleed.

The diagnosis is promptly made by the examination of the stools or by introducing the rectal tube and examining some of the bloody stained mucus, when the characteristic organisms are easily discernable. By examining the fresh specimen while it is still warm the parasite is found to be very active, but it becomes more sluggish as its surroundings become colder.

The duration of the diarrhea in patients known to be infected with the parasites has been as long as fifteen years.

All the reported cases, with two exceptions besides this one, have been in adults. The age of this patient is next to the youngest recorded, the other two being 4 years and 5⅓ years, respectively.

The prognosis depends on the ability to rid the host of the balantidia. Many cases are shown wherein the relative decrease in the numbers of the parasites is coincident with a corresponding improvement of the patient.

Remembering the pathology of the disease, with its possible complications in the liver and lungs, it may be said that the earlier the diagnosis and the more thorough the treatment the better the prognosis. The mortality has been given as high as 30 per cent. by Strong.

From the information available the prophylaxis should be directed toward the care and hygiene of those who are in close contact with the care of swine and the manufacture of pork products, and the thorough cooking of the pork products before ingestion. If to this is added a safe water supply, prophylactic measures against this infection will be as complete as our present knowledge will warrant.

Many drugs have been employed in the treatment of this infection, mostly by colonic flushing and by enema. Quinin, tannic acid, silver nitrate, iodin, acetic acid, salicylic acid and boric acid, methylene blue, thymol in olive oil followed by castor oil, have all been employed. By mouth arsenic and thymol have been used.

There is as yet no known specific in the treatment of this disease, but because of the resemblance of this infection to that of amebic dysentery: (1) in the invasion and location of the organisms in the tissues; (2) in the histologic pathology; and (3) in its clinical manifestations, it would seem that ipecac or its alkaloid, emetin, should be employed, as it is hardly to be expected that local flushings will be of any avail after the infection is established.

If in reporting this case I may only have stimulated interest as to the possibility of this parasite being a cause of frequent stools and placed the physician on guard for the recognition of this infection, which has been shown to exist not only in tropical and subtropical climates, but in the colder climates as well, where the symptoms are less severe, I will feel that the purpose of this paper will have been subserved.

NOTE.—Since writing this paper another case has come to my knowledge in which emetin was employed in its treatment, and, I am told, with spectacular results.

PROGRESS IN PEDIATRICS

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IMMUNITY REACTIONS IN HYDRATED AND CONCENTRATED TISSUE *

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MINNEAPOLIS

That certain types of organisms succumb more readily to the invasion of disease than others is an old clinical observation. This gradually crystallized into the expression that the apparently fat, plethoric organism showed on the whole a lesser degree of resistance than the lean, fairly emaciated organisms. This experience is quite strikingly borne out in two familiar disease processes; the pneumococcus infection and tuberculosis.

If one will look on certain types of obese organisms as having tissue with a larger water content than the thin, lean organism one may use the expression that in the former case we are dealing with hydrated tissue and in the latter case with concentrated tissue. That hydration or concentration of tissue bears some definite relationship to immune reactions unfavorable in the hydrated and favorable in the concentrated tissue is a thought which has repeatedly been expressed in the literature.

REVIEW OF THE LITERATURE

Among pediatrists, Czerny[1] and his followers have mentioned the possibility of this connection and have published some interesting observations bearing on the point. Czerny emphasizes the connection existing between a state of nutrition and the natural immunity of an organism, and states in fact, that natural immunity is dependent on the state of nutrition. He points out that there are differences between the natural immunity of different tissues and organs and explains in this way the localization of infectious disease processes.

Congenital factors can affect the development of immunity as well as changes wrought during the advancing age of the tissue.

Czerny finds that natural immunity is least developed in the premature, very slightly during the first few years, and shows a maximum

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[1] Czerny, A.: Med. Klin., 1913, No. 23, p. 895.

development during adolescence and middle age. From clinical experience he comes to the conclusion that the infant who can tolerate the largest amount of fat in his food shows the best natural immunity. High carbohydrate feeding while generally well tolerated, lowers immunity to an unusual degree. Infants with a higher water content in the tissues are very vulnerable to infection. Premature and newly born infants are easily infected. There is little tendency to localization. The infection quickly becomes general. The infection with tuberculosis, for example, is a striking instance.

In this connection the experimental work of Weigert[2] on young pigs infected with tuberculosis is interesting. He found that the pigs fattened on high carbohydrate feeding whose tissues were in a state of hydration, as it were, showed an exceptionally low resistance to the infection as compared with normal pigs or those fed on mixtures predominating in fat content. Weigert believes that there is a definite connection between natural resistance and the water content of the tissues. It is probably one of a series of biologic physical or chemical factors which influence or modify the constitution of the organism and on which immunity depends.

The laws governing the behavior of the water content of the tissues of various animal species are today still the same as those expressed and formulated by V. Bezoldt[3] over fifty years ago. Every individual animal organism has a content of water, organic material and inorganic salts, typical for its age and species. This is either nearly constant or it may vary between wide degrees.

The growth and development of every animal is characterized by changes, typical for each species, in the composition of the above named components. These changes are principally:

(a) Decrease in the organism of water and volatile components from the embryonal stage until the period of free growth.

(b) Increase in content of solid inorganic material. This increase being particularly rapid for the first period after birth.

(c) A steady growth, although extremely slow during the first period of life, of the ash content. This growth continues until the completion of the period of progressive development.

Weigert's[4] experiments confirmed generally the above laws. He concludes that the water content of the animal's tissue depends on its age and nutrition. Variations of the water content are not alone determined by increase or decrease of the fat content of the animal organism, but are also determined by a varying content of fat-free, dry substance. The increase of fat-free, dry substance involves equally the content of nitrogen and ash. Animals fed on protein and fat-rich food show the largest content of fat-free, dry substance. Applying his results to the infant organism, Weigert concludes that the breast-fed infant's organism has a lower water content than the artificially fed on account of the greater fat percentage of breast milk.

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[2] Weigert, R.: Berl. klin. Wchnschr., 1907, No. 23, p. 1209.

[3] Bezoldt, V.: Ztschr. f. Wissenschaftl. Zool., 1857, **8,** 487.

[4] Weigert, R.: Jahrb. f. Kinderh., 1905, **61,** 178.

The coincidence of diminished water content of the organism with increased resistance to infection explains the natural immunity of the breast-fed infant. The question here might be raised whether this is the only factor operative in this higher degree of resistance. It is now a known fact that immune bodies can pass from the mother to the nursing offspring through the breast milk.

R. Lederer,[5] studying the relationship of water to constitution and nutrition, reports the interesting finding that one-sided feeding of young animals on cow's milk, dogs in this case, caused the normal, physiologic dehydration of the growing organism to remain stationary, or even could cause increase in the water content of the blood. Excessive intake of fluid along with other food could delay the drying out of the organism. The same thing could be accomplished by continuing breast feeding beyond the physiologic period of weaning. Lederer finds that the curve of physiologic dehydration shows an abrupt interruption shortly after birth. The water content of the blood of the new-born increased from birth until about the middle of the third month. From this period on, the slow physiologic dehydration continues to adolescence.

These findings are of some interest in connection with the view expressed by Czerny in reference to immunity in the young, under conditions of natural and artificial feeding. A part phenomenon of natural immunity is the capability of the organism to react to an infection with the formation of specific immune bodies. Most of the recent experimental work has for this reason been along immunologic lines, and has concerned itself with a search for these immune bodies and with a study of their behavior under varying conditions.

Moro[6] found complement in the serum of the fetus and the newborn in an amount virtually equal to that of the adult. In the breast-fed infant it reaches this amount as early as the fourth or fifth day, and remains quite constant. The conditions are much the same in the artificially fed infant, except that there are variations in the amount and frequently diminution. He found the complement content of the atrophic infant and those suffering from alimentary disturbances far below the normal, and found that it could be markedly influenced by nutrition.

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5. Lederer, R.: Ztschr. f. Kinderh., 1914, **10,** 365.
6. Moro, E.: Monatschr. f. Kinderh., 1907, **6,** 340.

Adair[7] found hemolytic complement in the new-born babe and could demonstrate it in fetuses as early as the eighteenth week of fetal life. It was present in smaller amounts in the fetal than in the maternal serum. He concludes from his experiments that the hemolytic complement is developed in the fetal blood and that the amount developed is controlled by the fetal organism.

Heiman[8] found the actual and potential complement content of the blood reduced in the artificially fed infant. Kaumheimer[9] could not corroborate the findings of Moro, but found the complement content high in the organism favored with an apparently normal constitution, but distinctly lower in the organism with abnormal constitutional manifestation.

E. Thomas[10] and O. Horneman[11] carried out a series of experiments on pigs analogous to those reported by Weigert in this case, however, determining the immune reactions on young pigs infected with tuberculosis and subjected to various feeding conditions. These observers found that pronounced variation in the feeding had no influence on the complement content or the opsonic index. Both the infected and noninfected animals showed no difference in the complement content. They corroborated the findings of Weigert that high protein feeding retarded the spread of the infection whereas high carbohydrate feeding favored it.

Kleinschmidt[12] studied the antibody formation on young dogs under both natural and artificial feeding conditions. Hemolysis and agglutination were the reactions principally determined. He found that neither high carbohydrate nor high fat content of the artificial food influenced antibody formation to any degree. Alimentary disturbances, however, can hinder antibody formation. Marked disturbance of the antibody formation occurring during an alimentary disturbance can quite rapidly be brought back to normal during the repair stage if the animal is placed on natural feeding. During the repair stage, for example, the hemolysis can be practically normal, even if the body development is markedly retarded. Kleinschmidt concludes from his experiments that the constitution of the organism is more important by far for the development of immune reactions than is the type of feeding.

P. T. Müller[13] studied the influence of artificially produced alter-

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7. Adair, F. L.: Tr. Am. Gynec. Soc., 1915.
8. Heiman: Monatschr. f. Kinderh., 1907, **6,** 340.
9. Kaumheimer, L.: Centralbl. f. Bakteriol., 1909, **49,** 208.
10. Thomas, E.: Biochem. Ztschr., 1913, **57,** 456.
11. Horneman, O.: Biochem. Ztschr., 1913, **57,** 473.
12. Kleinschmidt, H.: Monatschr. f. Kinderh., Ong. 1914, **12,** 423.
13. Müller, P. T.: Arch. f. Hyg., 1904, **51,** 365.

ations in the metabolism on the production of antibodies. One series of doves was fed on food rich in fat and protein, and a second series on food rich in carbohydrate and deficient in protein and fat. The animals were then subjected to infection with different types of organisms. He could not show definitely that the type of feeding had any consistent influence on antibody production. For some organisms it was marked, for others not. Much seemed to depend on the nature of the micro-organism that was used as the infecting agent.

Trommsdorff[14] studied factors which would tend to reduce the natural resistance of the organism to infection. His work was carried out on guinea-pigs. In connection with the present study his results from the effect of starvation on production of immune bodies are particularly interesting. Trommsdorff comes to the conclusion that starvation has an unfavorable influence on the production of antibodies. Prolonged periods of hunger would, for example, diminish hemolysis or abolish it altogether.

Similar results were found by Bakunin and Boccardi[15] who found the alexin content of the blood of starving dogs and doves reduced or absent. Meltzer and Norris,[16] on the other hand, did not find that the bactericidal faculty of the blood serum of starved dogs was decreased. Rosatzin[17] found no change in this respect in rabbits deprived of food and water. Roger and Josue,[18] and Teissier and Guinard[19] observed that withdrawal of food paramount to starvation would at first lessen the animal's organism resistance to infection. If the starvation, however, was not carried to extremes and was continued over a long period, the animals were found to be much more resistant than the control animals.

AUTHOR'S EXPERIMENTS

The work I wish to report was undertaken to show whether there was any difference in the defensive mechanism of hydrated or concentrated tissue, using determinations of immune reactions as an index.

Parallel series of guinea-pigs were taken, as near as possible in age and weight for each series. The animals were kept under the best conditions possible. The preliminary feeding stage covered a considerable period before immunization. In the fat series, the attempt was made to cause increase in weight as rapidly as possible through the use of liberal carbohydrate feeding, particularly maltose. The weight increase occurs rapidly if the pigs are kept under favorable conditions. Some allowance must, of course, be made for normal growth. The lean series of pigs were kept on a balanced ration just sufficient to sustain them. The development of scurvy was prevented by the use of moderate amount of fresh vegetable matter. The weight loss was brought about gradually and, before immunization, generally amounted to from 25 to 35 per cent. of the original body weight. The pigs were sound and active and showed no external evidence of disease. On account of the difficulty at present in obtaining material, the series tested for agglutination was on a shorter preliminary feeding period than the animals used in the other series.

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[14] Trommsdorff, R.: Arch. f. Hyg., 1906, **59,** 1.

[15] Bakunin and Boccardi: Riforma med., 1891, No. 188.

[16] Meltzer and Morris: Jour. Exper. Med., 1899, **4,** 131.

[17] Rosatzin: In Lubarsch. Zin Lehre von den Geschwulsten in Infect. Krank., Weisbaden, 1899.

[18] Roger and Jossué: Semaine méd., 1900, No. 29, p. 235; Compt. rend. Soc. de Biol., 1900, **52,** 696.

[19] Teissier and Guinard: Semaine méd., 1897, p. 67.

The lysin reaction was compared in fifteen fat animals and eighteen lean animals. The animals were immunized against blood cells by intraperitonal inoculations. About one-fourth c.c. of washed blood cells were injected intraperitoneally at from two to three day intervals. Two weeks following the third or fourth injection the animals were exsanguinated, the blood allowed to clot, and then centrifuged in order to separate the serum from the clot. The serum was then diluted with salt solution 1 : 10, and its lytic titer determined in the usual way. Objections might be made to this method on the ground that the serum of various guinea-pigs may not have contained the same amount of complement. It is a known fact that complement and amboceptor may replace each other within certain limits. However, it seemed that this was a more accurate method than to inactivate the serum in order to destroy the complement, as in the operation of inactivation, an appreciable quantity of antibodies is destroyed.

The precipitin reaction was carried out on eleven fat and eleven lean animals. The animals were treated with from one-fourth to one-half c.c. of ascitic fluid or human blood serum intraperitoneally as was done with the lysin pigs. The precipitin titer of the serum was then determined by the dilution method.

The agglutination was determined in seven fat and seven lean animals. The procedure was much the same as in the precipitin reaction. Pigs were inoculated intraperitoneally with a twenty-four hour killed culture of the typhoid bacillus. Four injections were made at three or four day intervals. Ten days following the last injection the titer of the serum was determined by the dilution method.

RESULTS

From the accompanying tables it can be seen that the lysin reaction was negative or nearly so in practically all of the fat animals, but was positive, sometimes to a marked degree, in over 60 per cent. of the

TABLE 1.—Comparative Results of the Experiments Undertaken to Determine the Lysin Reaction

Fat Animals (High Carbohydrate Feeding) (Immunized with Sheep Cells)				Lean Animals (Balanced Ration) (Immunized with Sheep Cells)			
	Initial Weight, Gm.	Final Weight, Gm.	Hemolysis		Initial Weight, Gm.	Final Weight, Gm.	Hemolysis
Series I				Series I			
Pig 1	280	630	0.08	Pig 13	250	190	0.04
2	355	840	No hemolysis	14	335	200	0.06
3	320	865	0.06	15	305	185	0.06
4	270	665	0.08	16	275	195	0.08
5	300	870	0.06	17	315	210	0.08
6	310	785	0.08	18	295	185	0.06 partial 0.05
Series II				Series II			
Pig 25	400	700	complete 0.06 partial 0.04	Pig 30	480	310	0.04
27	375	780	complete 0.1	32	435	350	0.06
28*	405	615	complete 0.04				
Series III				Series III			
Pig 40	345	825	No hemolysis	Pig 41	460	365	0.08
43	425	920	0.08	42	395	250	0.06
45	450	940	0.06	48	360	250	0.03
59	395	985	0.08	49	405	295	No hemolysis
				60	400	290	0.02
				61	415	325	0.04
Series IV				Series IV†			
Pig 52	265	655	0.08	Pig 54	335	350	0.08
53	270	600	0.08	55	450	515	0.06
				57	390	370	0.08
				58	400	385	0.06

* Pig had lost 235 gm. in past two weeks.
† Stationary weight.

TABLE 2.—Results Obtained in Determining the Precipitin Reaction

Fat Animals (High Carbohydrate Feeding) (Immunized with Ascitic Fluid)				Lean Animals (Balanced Ration) (Immunized with Ascitic Fluid)			
	Initial Weight, Gm.	Final Weight, Gm.	Precipitation		Initial Weight, Gm.	Final Weight, Gm.	Precipitation
Series I				Series I			
Pig 7	350	910	—	Pig 19	275	180	—
8	265	595	—	20	300	195	—
9	250	740	—	21	280	190	--
10	280	635	slight	22	305	185	slight
11	300	825	—	23	295	200	—
12	280	710	—	24	310	195	—
Series II				Series II			
Pig 33	385	635	trace, layer test	Pig 37	395	310	—
34	300	670	—	39	415	250	—
(Immunized with Human Serum)				(Immunized with Human Serum)			
Series III				Series III			
Pig 44	380	750	slight	Pig 50	415	250	—
46	610	1,035	—	51	435	385	—
47	435	830	—	62	390	295	—

lean pigs. The precipitin reaction was uniformly negative in both the fat and lean series. For some unaccountable reason the guinea-pig serum does not give the precipitin reaction. This is strange in view of the behavior of the agglutinin reaction, which while present in only 11 per cent. of the fat animals, was positive in over 70 per cent. of the lean animals. To draw far reaching or final conclusions from a study of this kind is surely unwarranted.

If, however, immunity reactions are a good criterion of tissue resistance the rather striking behavior of both the lysin and agglutinin reaction would seem to indicate that there is a difference in favor of concentrated tissue and that the theoretical considerations expressed by Czerny and other observers are substantially correct.

The author wishes to acknowledge the valuable assistance and helpful suggestions of Dr. W. P. Larson of the Department of Bacteriology and Pathology in the University of Minnesota.

CONGENITAL ATRESIA OF THE ESOPHAGUS

WITH REPORT OF FOUR ADDITIONAL CASES, WITH THREE NECROPSIES *

JOSEPH BRENNEMANN, M.D.
CHICAGO

In 1913 I[1] reported three cases of congenital atresia of the esophagus with necropsies which I had seen within a period of one year. In two succeeding years four additional cases have come under my observation. In my own experience no other congenital anomaly of the intestinal tract has approximated even remotely so great a number with the possible exception of hyperplastic stenosis of the pylorus. Among my colleagues (Drs. Richter, Grulee, Hess, Michael, Jackson and others) I have knowledge of at least six or seven more cases. In all of these cases there was identically the same clinical and anatomic picture. In all of them the upper end of the esophagus ended blindly, the lower end connected the stomach with the trachea — the so-called "inosculating" type of atresia of the older writers.

In 1884 Sir Morrell Mackenzie[2] collected 62 cases of congenital atresia of the esophagus and added one of his own. He placed the incidence of the "inosculating" type at about 70 per cent. In 1905 Kreuter[3] collected 98 cases, in only 64 of which it was reported that the esophagus was connected with the trachea, or a bronchus (65 per cent.). Cautley[4] in a recent (1917) somewhat less complete summary gives a detailed classification of type incidence of all congenital malformations of the esophagus, with a report of 85 cases of atresia, with about the same percentage of cases in which there was a connection between trachea and stomach as in the former reports.

My associate, Dr. W. Stanley Gibson, recently made an exhaustive search of all the literature on this condition. A full report of this review of the literature would detract attention from the main point of this short clinical paper, that is, that one type of atresia occurs with stereotyped regularity. Gibson found that since Kreuter's[3] sum-

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* Submitted for publication June 20, 1918.

[1] Brennemann, Joseph: Congenital Atresia of the Esophagus, with Report of Three Cases, Am. Jour. Dis. Child., 1913, **5,** 143.

[2] Mackenzie, Sir Morrell: Manual of Diseases of the Throat and Nose, 1884, **2,** 216.

[3] Kreuter: Die Angeborenen Verengungen und Verschliessungen des Darmkanales im Lichte der Entwickelungsgeschicte, Habilitationsschrift, Erlangen, 1905.

[4] Caûtley, Edmund: Malformation of the Esophagus, Brit. Jour. Dis. Child., 1917, **14,** 1.

mary, in 1905, some twenty or twenty-five cases have been reported, *all of which have been of the type here reported.* It is evident that in these cases there is a definite developmental anomaly that regularly follows a certain course, the exact nature of which is still in dispute and lies beyond our present discussion. Since practically all of the cases in the more recent and more exact reports have belonged to this one type, it has seemed to me worth while to report these further cases that exemplify this unity of type, and to emphasize the fact that for all practical diagnostic and therapeutic purposes congenital atresia of the esophagus is one definite clinical and anatomic complex.

The peculiar variation in the frequency with which these cases occur in the experience of different reporters suggests a further motive. Shukowsky and Baron[5] reported a case in 1912, the only one on record in a hospital experience of 50,000 new-born infants. The English pediatrician Cautley[4] reported a case in 1917, the first he had seen in "25 years of practice, mainly among children," and that " in the child of a Belgian refugee." Hirschsprung,[6] on the other hand, saw, and later reported, four of these cases within seven months while assistant surgeon in the Lying-in Hospital in Copenhagen, and reported five other cases, "two placed at his disposal by his chief, Professor Levy, one from the archives of the hospital," and two more observed later. Lotz[7] reported eight cases, specimens of which he found in the Pathological Institute at Giessen, and three of which had been reported previously.

The heaping of these cases in my own experience may serve as a further example. It is a very common occurrence in practice that a clinician who sees a rare case becomes interested in finding others and is soon rewarded in his search. It seems not unlikely that many more of these cases occur than are diagnosed. Possibly infants that have died in the first week or two of life because they were unable to retain food, or were erroneously reported as "vomiting everything," without showing evidence of pyloric or other well known obstruction, may have belonged in this category, and being only babies, who are supposed to do such things, have not been permitted even the consolation of an exact diagnosis. The diagnosis is singularly easy to any one who has the condition in mind or has ever seen a case. A colleague in a neighboring city recently sent me a reprint of his report of a case of the regular type which he had seen and necropsied, with

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5. Shukowsky and Baron: Arch. f. Kinderh., 1912, **58,** 191.

6. Hirschsprung, H.: Den Medfodte Tillerkning of Spieseröret, Inaug. Dissert., Copenhagen, 1861. Also, Cases of Congenital Atresia of the Esophagus, Hospitalstid., 1895, Part 4, **3,** 1037.

7. Lotz: Ueber die Kongenitale Atresia der Spieserohre, Giessen, 1910.

the comment, "This was the first case I saw after I got home from the Clinical Pediatric Congress in Chicago," where I had been fortunate enough to be able to demonstrate a living case. For this further reason I hope it is not without interest to call attention once more to this apparently not extremely rare condition, although it is regularly rated as such.

Anatomy.—The anatomy of this anomaly is shown in the accompanying figures. The upper end of the esophagus is uniformly dilated to a diameter of about 1 cm. or more, whereas the normal is about 4 to 6 mm., and ends roundly and abruptly at, or within, a centimeter above the level of the bifurcation of the trachea. The lower end of the esophagus is of approximately normal diameter, or slightly lessened. It runs directly from its normal location at the cardiac end of the stomach into the posterior aspect of the trachea at, or somewhat above, the bifurcation, or in a few cases it has been reported ending in a bronchus. This portion is usually from 4 to 7 cm. in length and commonly tapers slightly toward the tracheal end. In many cases it has been reported that a strand of dense "fibromuscular" tissue connected the lower end of the upper portion with the upper end of the lower portion. Thus Lotz[7] reports two such cases out of the eight that he reported. Others have reported a much higher ratio. The presence or absence of such a band is not always easy to determine, and little reliance can be placed on the published summaries with reference to this point.

Symptoms.—The symptomatology is strikingly uniform. An infant that in no way attracts interest to itself, pathologically, begins very quickly to unfold a series of symptoms that are pathognomonic and that could be predicted from a knowledge of the anatomic conditions. If the baby receives no food or water for some time after birth the first symptom is a constant slight flow of saliva from the more dependent corner of the mouth. If it is now put to the breast, or is given water it will swallow once or twice without any trouble. With every further attempt at swallowing the fluid will return in jets alongside of the nipple and through both nostrils. The child is now compelled to breathe with the mouth, nose and pharynx full of liquid. It suddenly stops nursing, its eyes become fixed, it rapidly turns blue and then struggles to empty its lungs by coughing. This is only gradually successful, and during this time it becomes deeply cyanotic, almost black. If it is not relieved either by its own efforts or by those of an attendant, it ceases to struggle, becomes quiet, stops breathing and is evidently drowning. Such an end seems relatively rare and is apparently a real danger only as the child gets very weak. If fluids are still given, unwisely, after the diagnosis is made, the baby will often toward the end make almost no attempt to empty the lungs, will simply become quiet and relaxed, stop breathing, become cyanotic and give up without a struggle. Probably in all stages some, and, at times, nearly all of the fluid that enters the lung escapes by way of the lower portion of the esophagus into the stomach, and this is doubtless another factor that makes immediate death from drowning so rare. The return to normal is greatly hastened at any stage by lifting the baby by the feet to an almost vertical position with the face downward so that the inhaled fluid can run out. After this has been accomplished it lies quiet and exhausted for some time, only to repeat the whole cycle again with each new attempt at nursing. It has been said that these attacks of suffocation occur independently of nursing, as a result of the vomiting of fluid from the stomach into the trachea through the lower portion of the esophagus. This has not been my experience except after gastrostomy, when fluid poured into the stomach for obvious reasons produces the same symptoms as when taken by mouth.

If milk has been taken it is mixed with the mucus from the nasopharynx as it is expelled and is whipped by the respired air into a fine whitish froth at the nares.

The stomach is slightly distended with air while the rest of the abdomen is flattened. This symptom has been present in every one of my cases and is important, as it establishes the fact that the stomach and trachea are connected.

For a few days the stools are normal in amount and are typical meconium. They then become scant, or absent, and if present are the typical greenish-brown slimy stools that characterize starvation.

After the second or third day there is an inanition temperature of moderate degree. This may persist throughout, or the temperature may become normal, or subnormal; it may or may not again rise as the aspiration or terminal bronchopneumonia that is always found at necropsy makes its advent.

The infant becomes rapidly weaker and more apathetic. Emaciation at first is rapid, then more slow, with a final loss of 25 per cent. to 40 per cent. of weight, depending on how long the child lives. The fontanel becomes depressed, the tissues dry and boardlike; the skin is drawn tightly over the hardened subcutaneous tissue, from which it can no longer be separated; the limbs are stiff; the face is drawn and fixed like a mask; the breathing becomes shallow and almost imperceptible; the cry becomes faint, high pitched and finally absent; the whole child resembles an automaton more than a living thing. Death is commonly so gradual that the time at which it takes place can hardly be fixed.

Death always occurs within two weeks. The average duration of life in this series was seven days; the three infants that were not treated surgically and represent more nearly the natural length of life of these cases, lived, respectively, eight, eight and ten days. Practically all of them showed at necropsy a terminal bronchopneumonia, for which conditions are peculiarly favorable here, but which seems to accompany nearly all deaths from marasmus in infancy. I am more inclined to think that the pneumonia is an accompaniment rather than a determining cause of death, and that those infants that are permitted to die naturally all die of starvation from the seventh to the tenth day. None of this series died from suffocation. While the latter form of death is probably wholly avoidable if all mouth feeding is withheld, which is, of course, the only course to pursue after a diagnosis is made, I do not believe that it presents as great immediate danger as observation of an acute attack might lead one to think it would. I am inclined to think that escape of fluid to the stomach through the lower end of the esophagus may be a most important factor in emptying the lungs, especially when the time comes that the baby is not able to expel the fluid through the mouth and nose.

Other congenital anomalies of all kinds are peculiarly frequent in association with atresia of the esophagus. Probably considerably more than half of the cases show one or more such accompanying abnormalities.

Diagnosis.—The diagnosis is very simple if one has the condition in mind, as practically all of the cardinal symptoms are present in each case. The attacks of apparently alarming cyanosis and suffocation when drinking are pathognomonic. The return of fluids from the mouth and nose, synchronous with the act of swallowing and always occurring after at most two swallows, is *sui generis,* and can hardly be mistaken for vomiting if it is seen. If one is sure that a baby has ever taken at one time one-half ounce of fluid by mouth without its immediate return, congenital atresia of the esophagus can be excluded. The flow of saliva from the mouth and the presence of a whitish froth at the nares should alone lead one to the diagnosis. The positive diagnosis as to the upper end of the esophagus is made by passing a sound or catheter. The normal distance of the cardiac end of the stomach from the lips in the new-born is about 17 cm. (Mackenzie[2]). In these cases there is abrupt and unquestionable obstruction to the passage of the sound, with a striking regularity at 12 cm. or a little less. That the lower end of the esophagus connects the stomach and trachea is established by the air-distended stomach.

A detailed description of three cases was given in the former article.[1] On account of the uniformity in all these cases, only brief descriptions of the present four cases will be given.

RREPORT OF CASES

CASE 4.—Baby B. Born on the service of Dr. C. E. Paddock at St. Luke's Hospital; colored; boy; mother had hydramnios; infant's birth weight was 6¼ pounds. The infant was abnormal in many ways: mongolian idiot; eyes not only typical of this condition, but less than one half normal size; palpebral apertures correspondingly small; smaller on left than on right side; ptosis of left eyelid; large toe and only three small toes present on each foot. It had all of the characteristic symptoms of congenital atresia of the esophagus. A sound could be passed only 11.5 cm., stopping abruptly. A slightly distended stomach established the diagnosis of the usual type of atresia. Gastrostomy was done on the sixth day; died four hours later. The infant lost 1¼ pounds in weight, about 25 per cent.

Necropsy.—This was conducted by Dr. A. L. Moody. The upper end of the esophagus was found greatly distended (1.3 cm.) and ended bluntly 4 cm. below the *rima glottidis,* and 1 cm. above the bifurcation of the trachea. The lower end of the esophagus was 6 cm. long and extended directly from the cardiac end of the stomach into the posterior aspect of the trachea 1 cm. above the bifurcation. It was about 4 mm. in diameter. The lower end of the upper and the upper end of the lower portion of the esophagus were at the same level and were connected by a firm connecting tissue.

CASE 5.—Baby E. Service of Dr. H. M. Richter, Wesley Memorial Hospital. Boy. The infant was 3 days old when it entered the hospital. It presented a typical history and appearance of congenital atresia of the esophagus of the regular type. A sound passed 12 cm. The infant died a few hours later, so there are no data as to weight, etc. Operation was performed by Dr. Richter a few hours after it entered the hospital. The technic and *rationale* of a new operation on this case are reported elsewhere by Dr. Richter[8] and will be discussed under treatment.

Necropsy.—The upper end of the esophagus was dilated to 1.5 cm. and ended abruptly 4.5 cm. below the *rima glottidis.* The lower end was 4.5 cm. long, about 5 mm. in diameter, tapering slightly toward the tracheal end, and extended from the cardiac end of the stomach into the posterior aspect of the trachea 5 mm. above the bifurcation. No other anomalies were found, but the examination was lmited to the region in question.

CASE 6.—Baby S. Service of Dr. L. J. Osgood, Wesley Memorial Hospital. Boy. Typical history and clinical findings. The sound stopped abruptly at 12 cm. from the lips; there was a drop in weight from 6 pounds 1½ ounces to 4 pounds, a loss of about 35 per cent.; there was a considerable elevation of temperature throughout after the first day or two. No operation was undertaken. The infant died on the tenth day.

Necropsy.—The anatomic conditions were carefully examined and found exactly as in the other cases. Both specimens and pathologic reports have unfortunately been lost, so that exact measurement and data as to other anomalies cannot be given.

CASE 7.—Baby S. This infant was brought to me by Dr. C. E. Smith of Beloit, Wis., when about 3 days old. Boy; birth weight 7½ pounds. The infant presented all of the typical symptoms. The sound stopped typically at 12 cm. This, together with the moderately air-distended stomach, established the diagnosis of the regular type of atresia. The father was informed of the essentially fatal nature of the condition and of the futility of attempting to relieve it surgically, and readily consented to take it home to let it die as peacefully as possible. The doctor reported later that the baby "died gradually on the eighth day." Necropsy was not permitted. This case was so typical in every way that there can be no doubt that the anatomic relations were the same as in the other cases. I would again emphasize the importance of a *moderately air-distended stomach with an otherwise flattened abdomen* in establishing the fact that the stomach and trachea are connected in a given case.

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[8] Richter, H. M.: Congenital Atresia of the Esophagus; an Operation Designed for Its Cure, with a Report of Two Cases Operated on by the Author, Surg., Gynec. and Obst., October, 1913, p. 397.

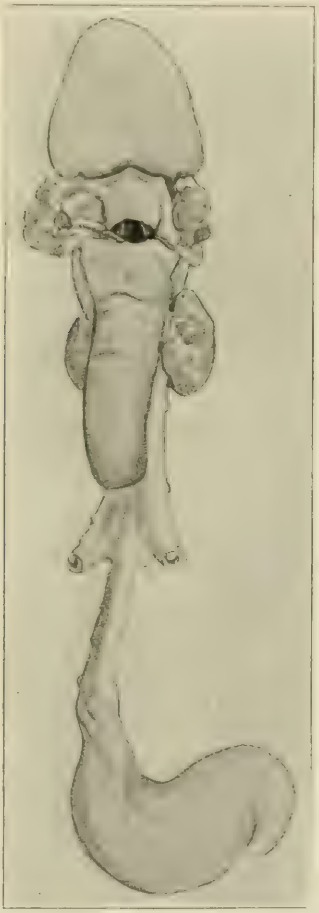

Fig. 1.—Congenital atresia of the esophagus, posterior view. Case 1, previously reported. The dilated upper end of the esophagus is shown extending from below the rima glottidis to the bifurcation of the trachea; the narrower lower portion from the stomach into the trachea at the bifurcation. Drawn by Miss E. Van Stoesser.

Treatment.—Congenital atresia of the esophagus has always been a fatal disease. Untreated the infants all die in the second week of life of inanition, or of a terminal or aspiration bronchopneumonia that is probably never absent; or, much more rarely, and only, I believe, if mouth feeding is continued, by drowning. Mouth feeding should, of course, be stopped as soon as a positive diagnosis is made, as it can only hasten the end through suffocation, or aspiration pneumonia. Rectal feeding is wholly inadequate in a new-born infant. At best it can prolong life a very few days.

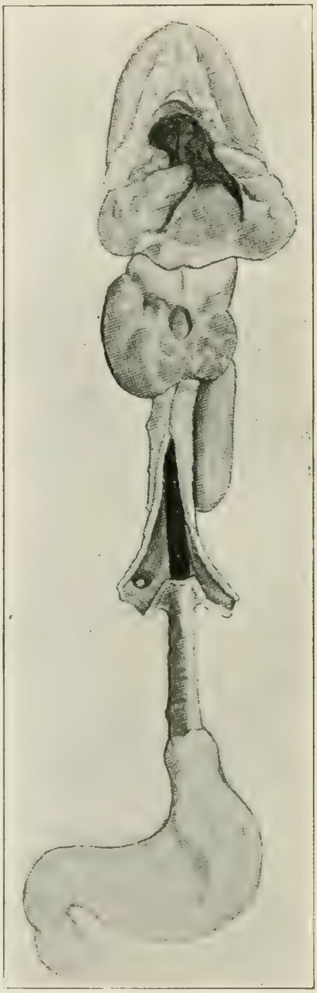

Fig. 2.—Same as Figure 1, anterior view. Upper dilated end of the esophagus partly hidden by the thyroid gland and the trachea. The lower portion of the trachea and the bronchi are laid open showing a sound (black) passing from the stomach through the lower portion of the esophagus into the trachea at the bifurcation. Drawn by Miss E. Von Stoesser.

The problem of treatment is to find some way to feed the child, and one looks to the surgeon for a route.

Surgical procedures have, however, so far served only to end more quickly a hopeless condition. While surgically successful, they are pediatrically impossible. It is practically impossible to nourish a new-born infant, nearly always already seriously undernourished when the diagnosis is made, when handicapped by the conditions imposed by any of the surgical procedures that have been tried.

Gastrostomy, recommended by Sedillot, has been performed a number of times (Steel, Hoffmann, Happich, Villemin, Kirmisson, Dickie, Demoulin, Richter, Halstead, etc.). In the light of our present knowledge that in practically all of these cases the stomach is freely connected with the lungs, this operation, unless accompanied by closure of the esophagus, no longer finds any justification. Fluids poured in the stomach quickly flood the lungs. The danger of drowning is far more real in this case than in mouth feeding, for in the latter the fluid can escape into the stomach while here it cannot. In fact, it becomes necessary after filling the stomach to hold the child erect and empty the stomach, or death will result. Gastrostomy, alone, is justifiable only if there is no connection between stomach and lungs, and no such case has been reported in over ten years.

Jejunostomy, recommended by Demoulin,[9] and performed by Dr. L. L. McArthur[1] in one of my former cases, would seem sounder, theoretically, at least. The objection again obtrudes itself that a new-born infant so handicapped cannot be nourished sufficiently to maintain life, to say nothing of building it up for a future more radical operation, without which life would be intolerable, even if it were possible. Furthermore, it would seem doubtful whether enough gastric and pancreatic juices that are essential to digestion could find their way into the distal portion of the jejunum, with a lumen so small as that of the small intestine of the new-born and with an opening as large as would be necessary for the introduction of food.

Two attempts have recently been made by H. M. Richter[8] to overcome the objection to the otherwise more serviceable operation of gastrostomy, by closing the upper end of the lower portion of the esophagus, at the same time doing a gastrostomy. The closure of the esophagus must be at the upper end both to save the esophagus for a later radical operation and also to obviate the blind pouch above the point of closure, the contents of which would quickly become dangerously infectious. This necessitates a formidable intrathoracic operation, in addition to the gastrostomy. Richter's[8] technic is given as follows:

> Preliminary gastrostomy under ether. Intubation of lower segment of gullet from below with metal sound. Change to positive pressure ether anesthesia. Incision in left seventh intercostal space, carried upward from posterior

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[9] Demoulin: Bull. Soc. de chirurgie, July 5, 1904.

end. Five ribs divided near their angles. A silk ligature carried around the gullet, using the sound as a guide. Seventh and eighth ribs brought together by a suture that included both (Sauerbruch). Intrapulmonary tension raised until lung came to chest wall, when remainder of wound was closed. Gastrostomy of the E. J. Senn type now completed and water immediately given through tube.

In the second case practically the same operation was performed, but on the right side instead of the left, as in the former operation. Richter[8] suggests, further, that instead of a simple ligation of the esophagus, "A more definite closure, with separation of the parts, is desirable. The part should be crushed with a heavy clamp, the crushed tissue cut, and both ends turned in." The first child died of shock shortly after the operation; the second child lived twenty hours and received 8 ounces of fluid at short intervals without evidence of flooding of the lungs. In both cases the ligation was successful, as shown in one case by finding the ligature in place at necropsy and in both cases by the fact that there was no suffocation or cyanosis when the stomach was filled.

If this operation can be performed on a new-born infant without death resulting from the operation itself, or from shock, or from infection either from the lower end of the esophagus in the proposed procedure, or from the blind upper end filled with bacteria constantly aspirated into the lungs, or from uncheckable starvation; then it offers some hope that the child can be made to live though always fed through a stomach fistula. The alternative would be a later operation aiming at a restoration of continuity of the esophagus, and the former ligation or separation of the esophagus would seem to add to the difficulty of this herculean task.

The ultimate ideal of all surgical attempts would be this union of the upper and lower portions of the esophagus. It is of interest in this connection that these commonly meet at the same level. Hoffmann[10] attempted this operation, approaching it, however, by the impossible neck route. He gave it up and did a simple gastrostomy, with the inevitable result. Whether this operation will ever be possible the future advances of intrathoracic surgery must decide. Even if possible, it would still seem probable that pediatric limitations will form an insurmountable barrier. In these otherwise hopeless cases, however, one gives the surgeon a full rein with a clear conscience.

When one considers, on the other hand, that nearly all of these infants have other anomalies; that practically all of them either have a bronchopneumonia or will almost inevitably get one if the upper portion of the esophagus is not drained into the lower portion; that a ***restitituo ad integrum*** of the esophagus does not yet seem feasible; that without this life, even if possible, would be intolerable; that the child could probably not be made to live even if successfully operated on for pediatric reasons; that no such infant ever has lived, no matter how treated, and finally, that parental sentiment must be weighed heavily in the balance, then if one, after careful counsel with the parents, decides to let the patient die as peacefully and painlessly as possible, one need lose no sleep because of that decision.

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[10] Hoffmann: Dissert., Greifswald, 1899.

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KALA-AZAR IN A CHILD (THE FIRST AMERICAN CASE) *

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History.—K. K., a girl, was born in Greece, Aug. 12, 1912. She entered the Children's Medical Service of the Massachusetts General Hospital, Aug. 15, 1916. Her parents were Greek, and reported that, although they themselves were well, they had lost the first two children, in Greece, of a disease similar to that from which this child was suffering.

The patient came to America in December, 1915. In January, 1916, she had pneumonia, followed by anemia and enlargement of the abdomen. Coincidently, she became weak and listless, and the symptoms became severe enough to bring her to the hospital.

Physical Examination.—The physical examination showed a pale, poorly nourished, white girl of normal intelligence. The head was symmetrical, and measured 48.5 cm. The pupils were equal and reacted to light. The ears, and ear drums were normal. The throat was normal. The heart dulness to percussion extended 2 cm. to the right and 6 cm. to the left of the midsternum. There was a slight systolic murmur over the precordia; the sounds were otherwise normal. The lungs were normal. The abdomen was very large, and when the child was prone, extended above the level of the thorax. The liver edge was palpable 4.5 cm. below the edge of the ribs in the nipple line. The spleen was very large, the tip being 4.5 cm. below and 3 cm. to the right of the umbilicus. The notch was easily felt. There were several patches of leukoderma, the size of a dime, on the chest. The reflexes were normal, and there was no enlargement of the peripheral lymph nodes.

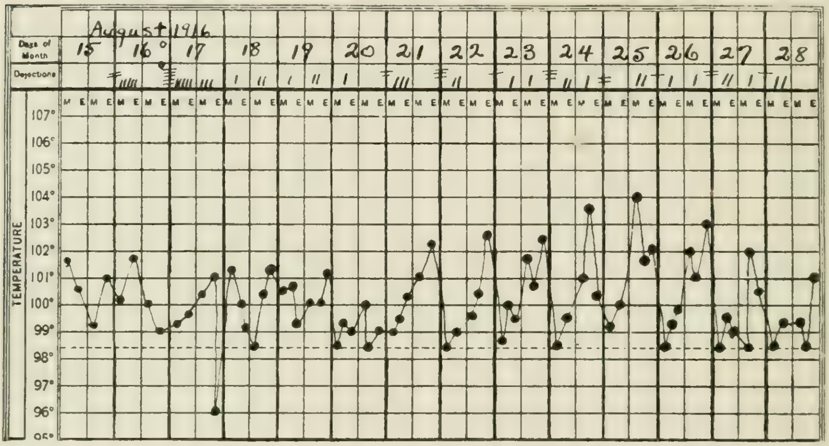

Fig. 1.—Sample of characteristic temperature for a period of two weeks.

The blood picture, shown in the accompanying table, with a low platelet count, 121, 324, led us to believe that we were dealing with an aplastic splenic anemia. The urine was normal on all examinations, except that now and then it contained the slightest possible trace of albumin, and a few red blood corpuscles. The temperature chart was found, later, to be characteristic in its irregularity. The accompanying four-hourly chart (Fig. 1) is a sample of two weeks which were typical of the course, during several months.

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* Submitted for publication June 4, 1918.

BLOOD EXAMINATIONS DURING THE COURSE OF THE DISEASE

Date	Hemoglobin	Red Count	White Count	Differential Count					Remarks
				Small Lymphocytes, per Cent.	Large Mononuclears, per Cent.	Polymorphonuclears, per Cent.	Transitionals, per Cent.	Eosinophils, per Cent.	
8/15/16	32 Dare	2,460,000	3,000	41	38	15	6	.	Reds slight achromia; very little variation in size; no malaria; no parasites or blasts
8/18/16	45 Sahli	2,240,000	2,800	52	28	15	5		
8/23/16	29 Dare	1,800,000	2,600	61	22	15	2		
8/31/16	29 Dare	2,000,000	1,600	61	22	15	2		
9/ 3/16	23 Dare	1,696,000	1,600	17	80	3			
9/10/16	30 Dare	1,676,000	1,500	61	24	15			
9/20/16	25 Dare	1,[illegible]60,000	1,600	42	37	20	1		
9/27/16	10 Dare	1,700,000	1,600	13	81	6	..	...	Two nucleated reds to 100 whites
9/29/16	....	....	......	..	..	..	..	...	Transfusion
10/ 1/16	50 Dare	2,400,000	4,000	16	76	6	..	...	Slight variation in size and shape; no blasts or Jolly bodies
10/ 3/16	50 Dare	2,800,000	4,800	34.5	34.5	25	5	...	
10/ 5/16	40 Dare	3,000,000	4,800	19	59	16	4	4	
10/ 6/16	....	....	......	..	..	..	..	...	Splenectomy
10/ 7/16	....	3,520,000	......	18	14	66	2	. .	Twenty-three normoblasts, seven megaloblasts, to 100 whites
10/ 8/16	70 Dare	....	5,000						
10/ 9/16	65 Dare	....	4,800	14	5	81			
10/12/16	....	....	7,500						
10/17/16	65 Dare	3,456,000	6,600						
10/21/16	....	2,912,000	6,800	..	..	..	..	...	One nucleated red
11/21/16	70 Dare	4,250,000	15,000	51	13	28	8	...	No nucleated reds
11/29/16	....	4,260,000	17,000	42	2	54	2		
12/15/16	70 Dare	4,500,000	18,000	47	2	51			
12/24/16	65 Dare	3,840,000	13,000	38	27	33	2		Six nucleated reds per 100 whites
1/ 1/17	70 Dare	3,968,000	12,500	30	20	43	7		
1/ 9/17	65 Dare	3,408,000	15,000	17	20	59	4	...	Number of normoblasts and stipple cells
1/23/17	60 Dare	3,288,000	14,400	31	7	55	7		
2/ 5/17	75 Dare	3,976,000	18,000	33	8	54	5	...	Achromia; polychromatophilia
2/13/17	75 Dare	4,432,000	20,600	35	3	54	4	. .	Some normoblasts; ++ platelets
2/23/17	75 Dare	3,864,000	18,400	22	7	57	4	3	
3/ 8/17	75 Dare	4,240,000	21,000	46	4	45	2	3	No nucleated reds, ++ platelets
3/28/17	75 Dare	....	20,000	71	1	25	..	3	No nucleated reds; platelets normal
3/16/18	95 Talq.	6,640,000	17,400	15	63	21	..	1	

Operation and Course.—Despite all treatment, the child lost weight and strength. Citrate of iron given subcutaneously was without any benefit. It was then decided to remove the spleen, but, because of the anemia, the operation was preceded by transfusion. Sept. 30, 1916, 200 c.c. of blood were introduced into the patient's anterior jugular vein by the indirect method (donor's blood, Group IV, patient's blood, Group IV).

October 6, splenectomy was performed by Dr. Beth Vincent, and a spleen, weighing 330 gm. was removed. The average weight of the spleen at 4 years is 42 gm.[1] The convalescence from the operation was without incident (Fig. 2).

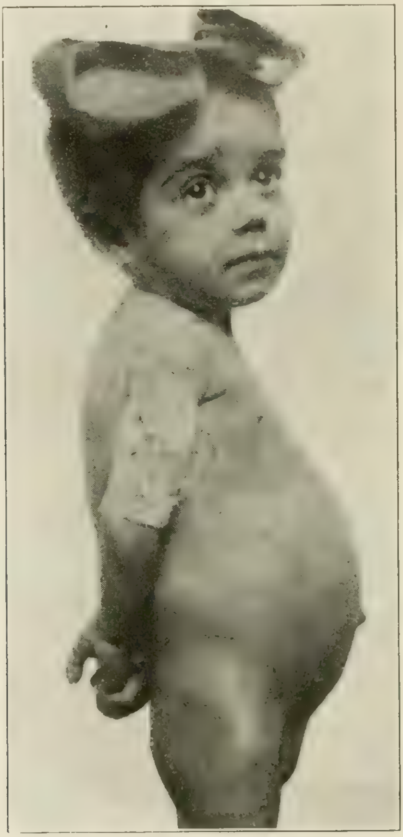

Fig. 2.—Photograph of authors' patient taken Feb. 5, 1917, four months after splenectomy.

Examination of Spleen.—The spleen on section was firm, of a reddish color, and showed small, whitish areas scattered throughout. A striking feature of the hematoxylin stained section was a large endothelial phagocyte cell filled with dark blue staining spherical figures of fairly uniform appearance (Fig. 3, colored plate). There were large numbers of these cells scattered throughout the splenic pulp. Smear from the spleen, stained with Wright's blood stain, showed bodies about the size of blood platelets. These bodies had a sharply

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[1] Gundobin: Die besonderheiten des Kindesalter, Berlin, 1912, p. 172, Table 36.

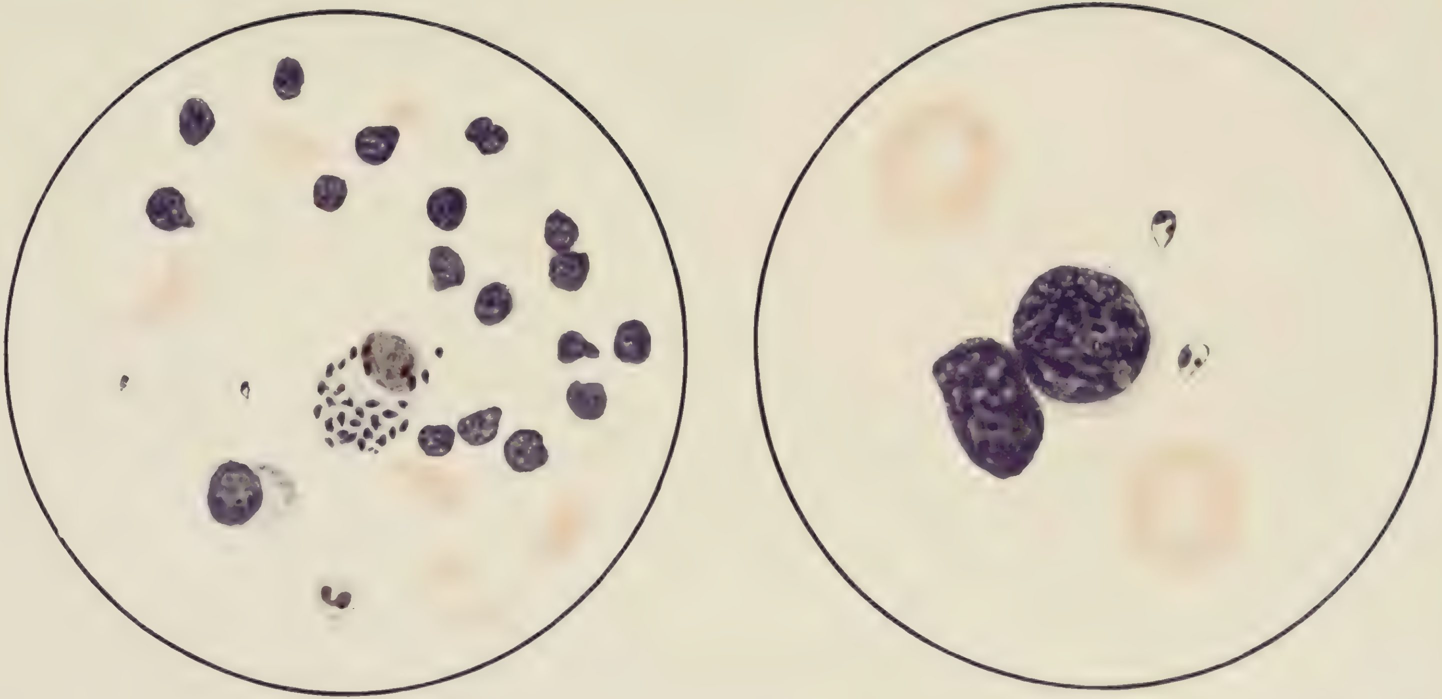

Fig. 3. Kala-azar. I. Actual field. Smear from fresh spleen showing many of the Leishman-Donovan bodies enclosed in a large endothelial phagocyte. (Wright's stain.) II. Morphology. Single Leishman-Donovan bodies compared in size with lymphocytes and red corpuscles. (Wright's stain.)

outlined, blue-staining periphery, and an unstaining central portion, which contained two purplish staining structures. One of these structures was generally oval, sharply outlined, and occupied a part of the periphery. The other structure was smaller, more intensely stained, and had a red shape. These bodies were identical, in microscopic appearance, with *Leishmania infantum*.

Following the removal of the spleen, the child was noticeably better; she gained in weight and color, and was much more contented and happy. A blood culture at this time (October 31) was negative. A small inguinal gland was removed for diagnosis, and from it Dr. A W. Sellards was able to cultivate high, motile, flagellated organisms in large numbers (Fig. 4).

Subsequent Treatment and Outcome.—Intramuscular injections of atoxyl were given, beginning November 2, for one month, without any apparent effect on the course of the disease. She subsequently commenced to lose weight and strength rapidly and continued to run an irregular, intermittent temperature. The liver continued enlarged.

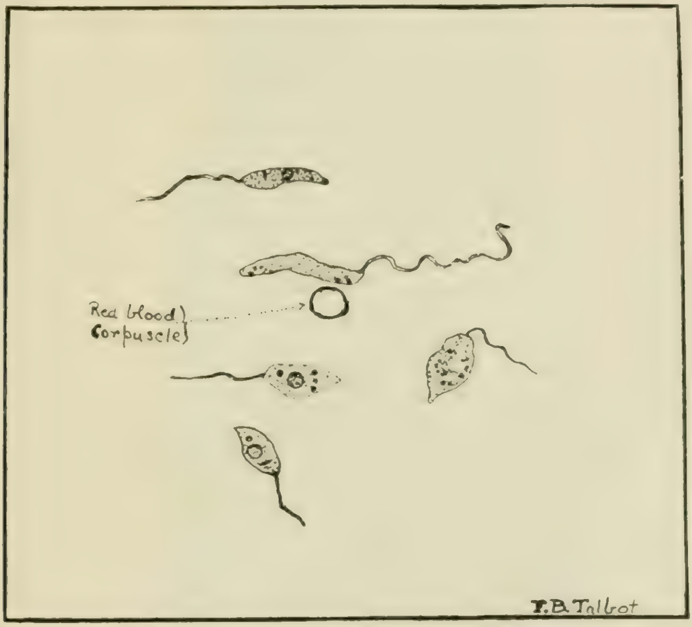

Fig. 4.—Culture of Leishman-Donovan bodies from inguinal gland of patient, K. K.

Following the suggestion of Sir Leonard Rogers,[2] a course of intravenous tartar emetic was commenced December 8. At first 1 c.c. of a 2 per cent. (0.02 gm.) solution was given daily, and later every other day, in increasing amounts up to 0.08 gm. When the tartar emetic was commenced the daily temperature varied between 99 and 104 F. One month later it had gradually subsided, and remained normal, with the exception of four days, until the child was discharged from the hospital. At one stage of its administration she was bothered by a cough, salivation, and loss of appetite, was irritable and cross, and remained in bed all day. The tarter emetic was, therefore, omitted; the appetite commenced to improve and the other symptoms cleared up. In the meantime an abscess had developed at the site of one of the tartar emetic injections, causing the child considerable discomfort. After this was drained there was a marked and continuous improvement in general health and weight; she started to play around the ward and the size of the liver diminished, so that, on discharge, it could only be felt 2 cm. below the edge of the ribs. The child was discharged from the hospital apparently cured, March 28, 1917.

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[2] Rogers: Lancet, London, Nov. 4, 1916.

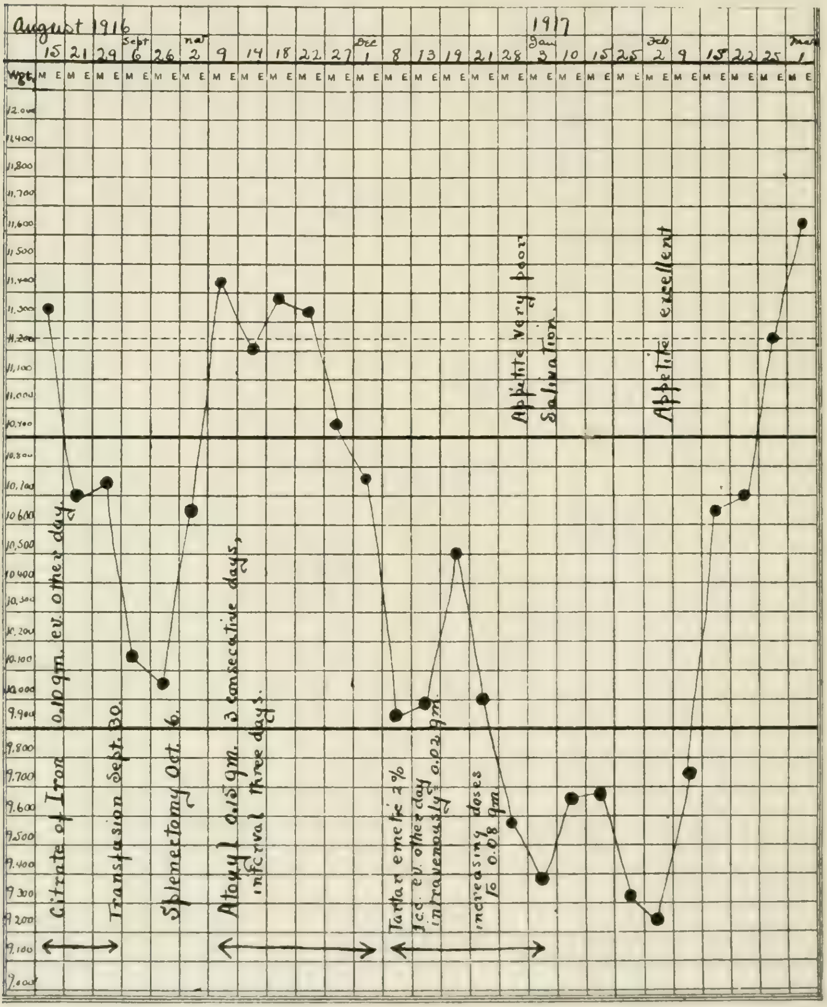

Fig. 5.—Weight chart, showing operations and medication.

The accompanying weight chart (Fig. 5) shows the operation and medication during the period the child was in the hospital.

The child was seen in March, 1918, after having been home for one year. During the interval she was perfectly well, with the exception of having had diphtheria. Her physical examination showed that she was now well developed and nourished, with no enlargement of the peripheral lymph nodes, except a very small gland in one groin, the size of a Number 8 shot. The heart, lungs and abdomen were normal. There were no masses felt. The liver edge was palpable just under the edge of the ribs. Her height was 94 cm., and she weighed 34½ pounds. So far as could be determined, she was an absolutely normal, healthy, well child (Fig. 6).

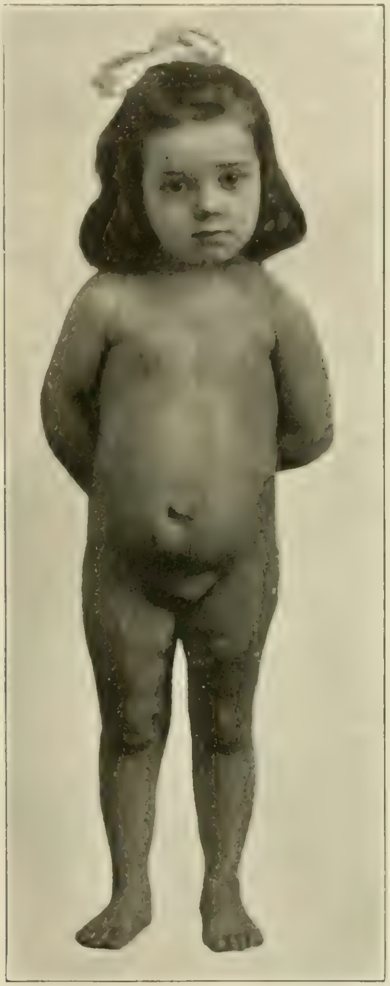

Fig. 6.—Photograph of child taken March 18, 1918, after having been home for one year.

DISCUSSION

So far as the authors know, this is the first case of infantile kala-azar reported in America. The disease is common in India, Asia Minor, and along the shores of the Mediterranean Sea. A few cases have been imported to England from these countries.

The parasites which bear the name of the Leishman-Donovan bodies were discovered by these investigators in 1903. They are also found in dogs, and it seems probable that fleas transmit the disease from dogs to man.

The incubation period is variable. It may be as short as ten days or as long as several months.

The onset of the disease is usually insidious, but it may commence with chills and high fever. The fever is intermittent or remittent, the temperature chart often showing two remissions in twenty-four hours. The fever tends to last six weeks or longer and then declines. During the period of pyrexia the spleen and liver become enlarged, and through the course of the disease there is progressive loss of weight and increased anemia.

The duration of the disease varies, death usually occurring within a year from weakness or some complication. The prognosis is, therefore, bad.

Treatment up to date has been unsatisfactory. Tartar emetic 2 per cent. solution, may be given intravenously, as recommended by Rogers. It is impossible to say whether K. K. was cured by the tartar emetic or not, but the permanent improvement seemed to result from its administration. Further observations confirming these findings, and those of Rogers,[3] must be made before it can be accepted to be of proved value. Improvement from splenectomy is, as a rule, only temporary. Other methods of treatment are without value.

311 Beacon Street.

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[3] Rogers: India Med. Gaz., 1917, **52,** July and August.

CURE OF A SYPHILITIC MENINGITIS BY ARSPHENAMIN AND MERCURY

SYMPTOMS—CONVULSIONS AND INTENSE OPTIC NEURITIS—DEVELOPED AFTER A HEAD INJURY *

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The writer presents the history of a case of luetic meningitis in a child. The condition, although not unusual, has received scant attention in pediatric literature.

REPORT OF CASE

History.—The child was well up to March 1, 1917, when he fell from the roof of a standing freight car, striking on his head. After the accident he seemed in great pain for several hours. During the night he had a chill and vomited until morning.

Two weeks later he commenced to have crying attacks and twitching and pain in the left arm.

These emotional attacks increased in severity and were associated with convulsions, which occurred every second night.

Four months after the injury (July 10) the patient entered the Buffalo General Hospital as a case of epilepsy. During the first ten days of his stay he had one convulsion, frequent screaming attacks and periods of maniacal excitement. He cried, swore and talked incoherently, and complained of pain and muscular twitching in his left arm. After a few days it was noticed that his movements were awkward and constrained; that he held his head and back very rigidly, the head being inclined to the right.

Examination, July 20.—He was a well developed boy of 10 years. The neck was very stiff and difficult to bend backward; no tenderness of the skull or neck; spine normal in contour but restricted in motion and very rigid; tenderness and muscle spasm along the vertebrae and in the right flank. A roentgenogram showed the cervical and dorsal spine to be free from disease The knee jerks were very active; ankle clonus of right leg; Kernig sign present, most marked on right side; muscles of arms and legs very spastic. The pupils were widely dilated; reacted to accommodation but not to light. There was a double optic neuritis of 2 diopters, each side. Leukocytes, 9,350; hemoglobin, 80 to 90 per cent.

By lumbar puncture 10 c.c. of fluid were obtained under moderate pressure: it was colorless, turbid and contained 466 cells per cubic millimeter. Globulin and albumin were each + + + +; Wassermann, + + + +. The father and mother each showed a Wassermann + +.

Diagnosis and Treatment.—The child was evidently suffering from a syphilitic cerebrospinal meningitis. He was given daily inunctions of mercury and arsphenamin every one or two weeks.

After the first dose of arsphenamin there was a prolonged chill and fever of 102 F., the only rise of temperature in the disease.

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* Submitted for publication June 12, 1918.

* Read at the Annual Meeting of the American Pediatric Societay, Lenox, Mass., May, 1918.

Course.—August 5. There were several screaming attacks and one long convulsion.

August 6. Swelling of the optic disks was much increased; most marked on the right side. The child said he could not see. There were severe root pains in left leg, right hip and shoulder.

August 10 to 26. During the next two weeks the child grew steadily worse. The screaming attacks and convulsions were very frequent. One day the child had four convulsions. He complained continually of root pain in his arms, legs and back. His mental condition was much disturbed. The child scarcely spoke at all; was slow of comprehension, disobedient, hard to control, executed simple orders slowly and with difficulty; often struck the other children in the ward.

The neck and back were very stiff. It was almost impossible to elicit lateral and backward movement.

Choking of the disk was very marked; right 4 D.; left 3 D., indicating increased intracranial pressure.

Spinal puncture gave 25 c.c. of fluid under pressure; very cloudy. Globulin and albumin were + + + +. The cell count was 1,700 (contrast with five weeks before: cell count 466), showing an increase in the meningitis.

August 27. No convulsions; severe root pains in the arm. The oculist stated that the optic neuritis was increasing and gave a bad prognosis as to vision.

September 3 to 6. There had been crying attacks and convulsions. Note that in the previous two weeks the convulsions almost ceased, but a steady increase in intracranial pressure was shown by the condition of the optic disks.

Two lumbar punctures gave no relief, and September 8, the oculist gave a last urgent warning that the swelling in each disk was 6 D., indicating dangerous intracranial pressure, and that blinding was imminent unless a decompression was made.

September 8. Decompression and aspiration of the right ventricle; 50 c.c. of fluid withdrawn. During the next ten days the child vomited frequently, was restless and screamed a great deal; no convulsions. The swelling of the optic disks subsided to 4 D., then increased to 6 or 7 D.

September 21. The right ventricle was aspirated; 15 c.c. of phenolsulphonephthalein solution were injected into the ventricle. Two hours afterward phenolsulphonephthalein was found in urine; two and a half hours afterward no phenolsulphonephthalein found in spinal fluid.

After the aspiration the boy was very restless for forty-eight hours and had a long convulsion, relieved by chloral. The optic disks were daily examined, but the aspiration produced absolutely no improvement. After two weeks a slow reduction in the swelling occurred. A month later the swelling amounted to 2 D.

There were no convulsions or mental disturbance after September 24.

October 22. The boy was in very good condition; ate and slept well; was active about the wards and out of doors. The mental dulness had disappeared; understood and obeyed quickly; was able to draw squares and circles, write name and address; was very responsive when given Swedish gymnastics; was mischievous and had to be frequently reproved.

Sensation was everywhere normal; head held to right; slight limitation of movements of head and spine; no local tenderness, neck, skull or back; mouth habitually open; pupils dilated; Kernig's sign present; knee jerk active; no ankle clonus.

Spinal fluid clear; 13 lymphocytes per cubic millimeter. Wassermann and colloidal gold test positive. Wassermann + + + + to 6 c.c.; negative to 0.4 c.c. Lange colloidal gold test = luetic curve, 1.5, 1.5, 2, 1.5, 1.5, 1, 1, 0, 0.

During November and December there was continuous improvement. About December 24, the Wassermann was negative, and the optic neuritis had disappeared. The boy was sent home and attended school regularly. In April he complained of frequent momentary headache. The spinal fluid, however, was negative to the Wassermann and colloidal gold tests. About May 1, the optic disks were normal.

On May 14, fourteen months after the beginning of symptoms, the child was free from all symptoms and had been for seven months.

INTERESTING FEATURES OF THE CASE

1. Neither the parents nor the child had any symptoms of syphilis, hereditary or acquired.

2. The fall on the head acted as a provocative agent causing cerebrospinal symptoms in a case of presumably latent hereditary syphilis. This, of course, is not unusual. Nonne believes that the importance of head injuries as a cause of cerebral syphilis is overestimated, and also says that these accidents do not cause especially severe forms of luetic meningitis; extensive affections of the interior of the brain may remain entirely symptomless. In the development of the brain symptoms of syphilis, nervous heredity or neuropathic constitution has absolutely no influence.

3. The lesion in the cerebrospinal meninges was probably a proliferative gummous leptomeningitis involving the cortex and spinal meninges; also in ependymitis with an increase of cerebrospinal fluid and some hydrocephalus. The choked disks were due to intracranial pressure from fluid and not to a direct inflammation of the optic nerve.

Optic neuritis is present in 40 per cent. of cases of cerebral syphilis. Ophthalmologists tell us that a high grade choked disk is usually a simple edematous saturation and may exist without disturbance of vision or injury to the retina, subsiding under antisyphilitic treatment. If the process is allowed to progress it may cause partial optic atrophy. In this case the course, increase and gravity of the brain symptoms was discovered and controlled by the oculist, Dr. H. W. Cowper. Every case of supposed epilepsy should have the fundus and spinal fluid examined.

Heubner emphasizes the frequency of epileptic convulsions in syphilis; of forty-five cases of gummous meningitis twenty-five patients had convulsions. Contrast the absence of fever with the fluctuating temperature of tuberculous and other meningitides.

4. The decompression and aspiration were followed by no immediate relief save that the lessening of intracranial pressure gave the cerebral circulation a little more freedom.

The patient was very responsive to treatment; the acute symptoms lasted about three months. Mercurial inunctions were given every day for five months and arsphenamin at first every week; later every two weeks.

The cure of syphilitic meningitis even before the days of arsphenamin was not infrequent. Of Nonne's cases of cerebral syphilis only two were between the ages of 1 and 10 and one between 10 and 20. All improved.

The same author using only mercury and iodid reports 71 per cent. of recoveries, acquired and hereditary syphilis having the same prognosis.

In syphilitic meningitis of the convexity, with partial and general epilepsy and alarming and characteristic symptoms, recovery is common. Relief is more certain if specific treatment is used early. Oppenheim and Ehrlich have the impression that in the present era of arsphenamin, cerebral symptoms are more frequent, owing to slight nerve injury rendering the tissue more susceptible to the irritation of syphilis. Oppenheim questions whether the Wassermann test of the blood and spinal fluid is a criterion for the continuance and repetition of therapy. The writer received much assistance in the management and treatment of the case from Dr. H. W. Cowper and Dr. E. H. Sharp.

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PSYCHOGENIC DISTURBANCES IN CHILDHOOD AND THEIR TREATMENT *

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Psychogenic diseases play an important rôle in childhood; they are at this period of life much more frequent and their nature is more easily demonstrated than in the adult; they are to a high degree subject to the influence of suggestion therapy and therefore possessed of a paramount importance in the practice of the pediatrician. The necessity of the recognition and appropriate valuation of the psychic elements in the complex of clinical syndromes cannot be emphasized enough.

DEFINITION

We understand by psychogenic diseases those disorders that emanate and originate from psychic processes, namely, from conscious, subconscious or unconscious ideas, associations, conclusions and impressions with or without accompanying emotions of the affected child. Though many of such disturbances are of hysterical nature, we must be cautious not to identify hysteria with the much broader term of psychogeny. Pain, fear, anxiety and worry, for instance, accompany in the adult perhaps every important somatic disease and lend a peculiar color to the clinical picture; their effects are closely interwoven with the purely organic symptoms through mutual interaction.

In the human mind there is a continuous current of mental processes, of associations, thoughts, ideas and conclusions and emotions, which to a great extent are underneath the surface of the clear consciousness, but which nevertheless leave residual imprints on the central nervous system, not always merely temporarily, but also of some duration and permanence in the form of subconscious or submerged memories and "facilitations." It was the merit of Freud and his school by his analytic methods to have brought the obscure, often deeply buried psychic elements and their intricate relation to somatic disturbances of neurotic character into the compass of scientific research and put them into a clearer perspective and better appreciation by the profession.

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* Submitted for publication June 22, 1918.

The psychogenic disturbances that are the subject of discussion in this paper may manifest themselves in the sphere of almost any organ, and the aspects of the symptoms are numerous and various. There is scarcely an organ that may not display nervous disorders of the nature of psychogenic reflex processes. They embrace the sensory, secretory and voluntary motor functions as well as those of the smooth muscles that are not directly subject to the will, as those of the gastro-intestinal tract and of the heart.

The psychomechanism, the methods of operation of the provocative occasions and agencies, and the sources of the disorders are of various nature. The latter may be due to imitation and psychic contagion, that is, have their cause in the "suggestion" or reflex receptibility which is a cardinal attribute of psychic life.

The special proneness of children to imitation, their great susceptibility to impressions, their impressionability on account of the immaturity, instability and undevelopment of character, the credulity, vivid imagination, belief in authorities and lack of logical criticism convert example, in their case, into a mighty, almost magic force, both in the psycho-physiologic as well as the pathologic direction.

IMPORTANCE OF EXAMPLE

In the presence of these peculiarities of the psychic life and on account of its tendency to discharge physical reactions on impressions, the environment or milieu of the child is possessed of momentous import. Therefore, no wonder that a disease, observed in another person, may be mirrored in the psyche and give rise to similar morbid symptoms in children. Particularly will a neurotic, hysterical person render others in contact with him, likewise nervous in the course of time, and the latter will often acquire and appropriate, as it were, certain nervous disorders and habits.

The danger of forming and stabilizing such nervous disorders, induced by the imitativeness and suggestion is, of course, with the child greater than with the adult.

We also frequently make the observation, that children affected with minor ailments will in different environments and surrounded by different persons present great variations in the clinical picture aside from the uniformity of the otherwise, of course, identical diseases, and act differently. Factors not lying within the nature of the pathologic processes themselves, but those of entirely extraneous characters, namely, the influences of the change of milieu, will call forth a change of the symptom complex in its nonobligatory, not organically caused, features; the impressionable plastic psyche of the child being affected by the transformative circumstances as clay or wax is shaped under the hand of the modeling artist.

The great historical examples of prodigious psychic epidemics, such as the children's migrations and crusades, the dancing manias, great choreas (St. Vitus' dance), etc., demonstrated the sweeping extent and overwhelming intensity of the suggestion, the power of example and the force of a "contagion idea" as Hecker, a physician, has depicted it with the pen of a historically and psychologically well trained writer.

Also the well known psychic school epidemics of our times, that are recorded in medical literature, give testimony to the great forces dormant in the human mind. For example, we cite the epidemiclike occurrences among many school children of the same classes of tremor, singultus, choreatic movements, disturbances of handwriting, enuresis nocturna, sleeplike states and other peculiar phenomena of the so-called imitation or induction diseases.

For the individual physician more important are the sporadic, isolated cases of psychogenic disturbances of imitative origin. They represent a great variety, they are protean and may affect the nervous system, the psychic sphere and the vegetative functions. As I have dwelt on this feature in a former essay, I may here only summarize, that in children in very numerous instances motor, sensory and visceral disturbances, such as for instance, attacks of limping, tremor of paralysis agitans with more or less exactness of the crude clinical picture, facial and other *tics convulsifs*, peculiar dyspneas or types of respiration, backache or pain in the chest, in the limbs, in the side or the abdomen, heart palpitations, vomiting, etc., could be traced to no other etiologic factor than to the suggestive influence of the example of their parents, most often the mother, who would complain day by day of their own ailments and pains, imaginary or real, in the presence of their children. The nervous parents through their conduct awake in the child corresponding ideas and impressions and guide its imagination in a certain pathologic direction. Such parents also by their anomalies of character in the sphere of emotion and volition are bound to be of immense educational detriment to their children, aggravating the effect of an hereditary neuropathic constitution by the influence of a morbid environment, the neuropathic milieu.

AUTOSUGGESTION

But perhaps more than the ailments of others do the child's own diseases influence its psyche. The subjective symptoms of an originally organic disease, as a rule painful or involving the motor function, will be aggravated or prolonged psychogenically. For instance, after a catarrhal laryngitis hysterical aphonia may follow; or after tonsillitis, that had kept the patient bedridden, abasia and astasia; or blepharoclonus may remain after the subsidence of acute conjunctivitis or the removal of a foreign body.

Pain, after the complete cure of its organic basis, will become fixed as psychalgia, as *douleur d'habitude* (Brissaud's), as habit pain; the latter will be, so to speak, the reverberation of the previously actual pain that accompanied some organic disease. Such disturbance represents a condition brought about by auto-imitation of the original disease; it is the psychogenic residue, "the declaration of permanence" (Bruns) of the subjective symptom of the previous organic disease.

After the disappearance of acute rheumatic polyarthritis, a psychogenic residual pain may persist for a long time and may even be of a very violent nature; these arthralgias may be so intense as to forbid the slightest touch while the child is aware of it, but will disappear entirely if the attention is diverted or in the sleep, so that the child will lie in any position on the affected part.

As classic an example as one could wish to demonstrate this condition is described in the following case:

O. A., a boy aged 5 years, had the following history: Three months ago he became ill with pains in various joints; the left knee particularly was swollen and reddened for awhile; it remained painful permanently. Two months later pains in the right knee, in the ankles and shoulder joints supervened. He had been three months bedridden, when he was admitted to the Cook County Hospital. The boy, when seen by me for the first time, manifested extreme pain on the slightest touch or attempt at passive movements of both hip and knee joints; they were contracted and held in moderate flexion. The feet were slightly painful to pressure. Swelling was not present anywhere. During sleep the contractures, however, disappeared and time and again the boy was found lying in any position of the affected limbs. There was also free passive mobility, if the child's attention was sufficiently diverted by various tricks. It was indeed a classic example of the psychogenic character of residual, though very vehement pain. After a few days the pain had disappeared completely, but the boy, while rather freely using his legs in bed where he liked to play cheerfully, was entirely unable to stand or walk, manifesting complete astasia and abasia. This astasia and abasia proved rather refractory, perhaps as a result of too much attention and interest shown to him in frequent clinical demonstrations. After about four weeks he rather unexpectedly was found standing up in his bed and climbing over the railing into his neighbor's with remarkable skill, but he was still unable to stand or walk on the floor. Then, for therapeutic reasons his legs were submerged in cold baths twice a day and within three days the control of his legs was restored.

Other patients manifest painful sensations or motor disturbances, as contractures and pseudoparalysis that persist obstinately subsequent to a perhaps insignificant trauma. Two instances that could be multiplied may suffice to exemplify the statement.

The 8-year-old son of an artist after a fall on his right shoulder during play suffered from vehement pain and stiffness of the joint for several days, when on examination no lesion could be found. The roentgen-ray examination revealed no lesion. The free passive mobility of the joint when his attention was distracted, and the rather sudden disappearance of pain and contracture after a merely suggestive treatment proved clearly the psychogenic character of this residual disturbance.

M. S., a girl, aged 12, three months ago when playing, fell forward on the pebbly ground in front of the school. Two days later dull pain in abdomen and headache of a shooting character appeared and has persisted in the form of daily attacks since then. The abdominal pain appeared independent of the meals and the headache occurred every morning and evening, continuing for about one hour; they were brought on or aggravated especially by excitement. There were no objective signs of any injury, but painfulness of the lateral and lower parts of the abdomen on pressure was present. A verbal suggestion emphasizing a complete cure in conjunction with abdominal massage on the spot, brought about the immediate disappearance of the pressure pain. A few drops of tincture of valerian were ordered daily. The headaches and pains in the abdomen never returned.

To show what queer pranks autosuggestion may play on a child, the following case exhibiting a component of phobia may be here reported.

An intelligent boy aged 7 had short but frequent attacks of a feeling of constriction in his throat and inability "to swallow the saliva," causing him "fear of choking." A swallow of water would forthwith relieve the distressing symptom. These attacks by their frequency caused him so much anxiety, that finally he was afraid to go where he would not be able to get water if in need. When outdoors he chose streets or places where he would find a well or pump nearby. On one occasion a more severe attack seized him suddenly in a long street, so he had to hurry to a well; drinking gave immediate relief; but as soon as he had left the well, another attack compelled him to return forthwith; this happened several times in close succession; it was only with apprehensive hesitation, that he ultimately went home. The attacks continued over one week. The boy was otherwise perfectly healthy.

The only explanation I could find of this peculiar disturbance manifested in this boy was perhaps either the possibility of a previous tonsillitis or more likely in combination with the fact, that the boy's phantasy had been much aroused by stories about "choking and impossibility of swallowing" in a case of hydrophobia that had occurred in the town.

The auto-imitation of a previous organic disease, the fixation of a symptom in the psyche, indeed often is directly cultivated and fostered by the overanxiety, morbid solicitude, apprehension, overindulgence and imprudence of some parents. They may by asking the child over and over again after this or that symptom keep the latter alive in the mind of the sick child, or they may yield to every desire and wish, however foolish, of the sick child out of excessive sympathy, and multiply their manifestations of parental care, so that there seems to the child to accrue more advantage from being sick than from being healthy.

This fact holds also true of the so-called oneirogenic (dreamproduced) disturbances of sleep; as for instance, of somnambulism. As is well known, nervous, especially hysteric children, may occasionally leave their bed due to restless sleep, vivid dreams or fears. If the parents show themselves unconcerned, as a rule the attacks will rapidly disappear spontaneously. However, if much concern is shown and apprehension expressed in the presence of the child, in a number of instances rising from bed and sleep-walking will become more frequent and the morbid tendency aggravated. By ignoring the condition and removing the child from his obnoxious home environment, these procedures, as a rule, soon correct the sleep disturbance, proving by the influence of suggestion its psychogenic nature.

COMPLICATING FACTOR

Not only may the psychogenic factor assert itself in prolongation of pain after the subsidence of the organic cause, but — as passingly said before—it may also during the organic stage of a disease by aggravation exaggerate the clinical manifestations, or add to the organic complex another complicating symptom which may be recognized as neurotic by the prompt effect of psychic treatment, as will be discussed later in extenso.

The following case will exemplify such an element of psychogenic complication of rheumatic chorea minor.

M. S., a Jewish boy, when admitted to the Cook County Hospital, manifested the symptoms of chorea minor of moderate degree. This was the third recurrence within two years. Lately, according to the history of the case, attacks of violent tremor of both upper extremities had supervened; they continued as long as two hours without cessation, and occurred on some days several times, particularly starting under the influence of excitement and anger. This "trembling" consisted of very rapid pronatory and supinatory rotations of both forearms, the extremities being held spastically extended in the elbow joints, and directed downward. This "trembling" evidently not belonging to chorea minor, never appeared in the hospital and thereby documented its accessory character. The analysis of the etiology made it appear as very probable that the tremor had developed originally from the ordinary tremor that accompanies the effect of anger and wrath.

It is probable that in childhood all psychogenic disturbances originate in some actuality, either in a real organic somatic disease, or in psychic traumas, especially in impressions and experiences that react through the reflex of imitation, or in physical traumas with psychic by-effects. It is not only the severe acute psychic traumatism, that as a provocative factor of neurotic disturbances comes into consideration, but often also the small, apparently insignificant, not dramatic psychic insults, that, if repeated, may have and do exert a cumulative effect. Thus, particularly in the school age, injustices on the part of teacher or schoolmates, disappointments of expectations, frustrated ambitions, excessive aspirations overstimulated by the parents, anxieties, fear of examinations, etc., may act as slight but continuous injuries on the sensitive psyche especially of predisposed, angiasthenic, vasoneurotic and impressionable individuals. They may give rise to various morbid manifestations as, for example, heart palpitations, precordial pain, vertigo, etc. Exciting scenes of an unhappy home life act in the same way.

REFLEX INFLUENCES

Many phenomena explained as due to auto-imitation and classified among the manifestations of monosymptomatic hysteria have to be considered as nothing else but "pathologic conditional reflexes," the definition of which Ibrahim has circumscribed, introducing it into our clinical terminology, in his exposé, following Pawlow's doctrine.

A typical example, representative of the conditional reflex of pathologic character is illustrated by the so-called pertussis tic, the "*tic coqueluchoide*" of Lesage and Collin. As generally known, especially neurotic children, suffering from whooping cough, will for an unduly long period, even for months, continue to have attacks of spasmodic cough; this with the exception of its nonproductiveness of sputum, will mimic the typical pertussis. The children, in a number of instances, may call forth these attacks voluntarily, in order to impress their anxious, apprehensive environment and enforce their capricious will. In other instances, the cough due to acute bronchitis or pharyngitis, if acquired weeks or months after pertussis, may likewise copy its type. Striking therapeutic results are to be obtained at this stage within a few days or even at once by the application of methods that act merely through suggestion and are so successfully employed in hysteria of childhood, as by intentional neglect, brusque commands, energetic orders to suppress the cough, if necessary with emphatic threat of punishment or other educational means. This fact characterizes the nature of the disturbance as an acquired "pathologic conditional reflex" (Ibrahim). The cough impulse constitutes the stimulus for the conditional, semi-voluntary reflex. The children need only produce a few cough impulses either purposely or impelled by broncho-catarrhal or pharyngeal irritation, in order to have started the entire mechanism. The rapid cessation of the attacks, once the child has succeeded in suppressing them a few times under the influence of therapy or by avoidance of their provocations, indeed is in keeping with the extinction of a conditional reflex in the animal experiments of Pawlow and his pupils, or in the experiments of Krasnogorski in children. The fundamental investigations and achievements of these authors, indeed, have thrown a bridge into a new field of fruitful and promising scientific research.

The conception of an acquired pathologic conditional reflex finds its ready application in "respiratory affect-convulsions," or rage spasm, the apnea in anger-paroxysms (Wegbleiben) of neurotic children. By suddenly springing a surprise, by diversion of the child's attention, by threats or a slight slap, such psychogenic paroxysms can be suppressed in the very start, as a conditional reflex in the animal experiment will be inhibited by the introduction of a new stimulus.

Also the not infrequent nervous vomiting of children in the morning before or on the way to school, may be traced to a psychogenic origin, perhaps under the cooperative, auxiliary influence of emotions, the psychic reflex act of vomiting being firmly anchored to the idea of going to school. In educating babies to defecate or urinate at a given regular time by bringing them on the chamber, we intentionally create a normal conditional reflex, the automatic act of defecation or urination becoming psychically anchored to this newly introduced stimulus. In many adults various sensory impressions, as, for instance, hearing water run, will facilitate the act of micturition, this acoustic stimulus, once established, serving here as an acquired conditional reflex stimulus.

In a boy, aged 5 years, for one and one-half years free bowel movements were obtained only every other day by a small enema; without the latter he obstinately refused to defecate. For him the enema evidently represented an acquired but apparently indispensable psychic stimulus more than anything else. The enemas for therapeutic reasons were completely discontinued, and after a few days of constipation the boy became convinced of his ability of spontaneous defecation, thus acquiring the normal habit.

The following neurotic disturbance, observed by me lately in the dispensary of the Rush Medical College may be cited.

A boy, aged 9 years, fond of school work, has suffered for several years from abdominal pain, that continues regularly from about 10 to 12 noon and from 2 to about 3:15 p. m. A close examination revealed, in addition to a slight diastasis of the recti muscles, rigidity of the abdominal walls and pain over the entire abdomen on pressure. The fact that the pain never appeared on Saturdays and Sundays or during the school vacations revealed the merely neurotic character of the disutrbance; its rapid improvement after a single application of the faradic current, and its complete disappearance within two weeks confirmed the diagnosis. The boy received a few drops of tincture of valerian daily.

ONEIROGENIC DISTURBANCES AND PAIN HALLUCINATIONS

It is a not sufficiently noted but very noteworthy fact, that also oneirogenic disturbances, that is, those due to the operation of dream-ideas or dreamlike states are amenable to the salutary influence of suggestive treatment, applied during the waking state. Not only pavor nocturnus, somnambulism and allied anomalies fall in this class, but also disturbances as illustrated in the following observation.

B. H., a girl, aged 11, suffering from headaches, awakes suddenly from her sleep between 10 and 12 p. m. with violent pains in the region of the stomach, but immediately after falls soundly asleep again. Sometimes this attack may occur in the same night a second time, rarely a third time. The attacks return at rather regular intervals of a fortnight during the past six months. For the past two days she also suffers from pains in the rectum, spontaneous and independent of defecation. Her brother suffers from enuresis nocturna. Inspection and digital examination of the rectum revealed no anomaly, but complete relief of pain resulted immediately. The definite disappearance of the nocturnal attacks of gastralgia and vomiting, for which no organic cause could be detected, on a mere suggestive medication (a few drops of syrup of ipecac) and verbal assurance of cure brings forth into clear view the psychogenic element of this disorder.

Oppenheim has called attention to the relation between certain pains, the so-called hypnalgias and the processes of sleep. A number of his adult patients had suffered from cardialgias or neuralgias that aroused them sooner or later after falling asleep and persisted only a short time after awakening, appearing again as soon as they yielded to the desire to sleep. These pains never began in the waking state. Whatever the explanation may be, in a number of his cases the origin of the disturbance has been, in the view of Oppenheim, probably due to pain hallucinations, that like other sensory illusions are in connection with dreams.

If attacks of fear, ringing in the ears, of pain or paresthesia exacerbate during the night, it may also be due to the patient giving them more attention to his somatic processes or because of the abrogation of the influences of the higher nerve centers.

Hamburger has turned his special attention to sleep disturbances in children, repeatedly observed also by Popper, of an oneirogenic origin, as whining, moaning and complaining, almost exclusively in the sleep, as abdominal pain, or vomiting or coughing attacks without awakening, that yielded readily to simple suggestive therapy (psychotherapy).

Such observations seem strongly to oppose the presumption, no more to be maintained, that pain, cough or vomiting, because occurring during sleep, must necessarily have an organic origin in every instance. Indeed, the sometimes striking curative effect of psychotherapeutic methods, as change of milieu, pedagogical influences, etc., in enuresis nocturna has long been an argument additional to those that likewise proved the correctness of the assumption of its inorganic origin.

TREATMENT

The psychogenic disturbances, with certain very obstinate exceptions, as a rule are very readily curable through various means that are essentially psychical. In psychotherapy we attempt to exert our influence on the idea, idea-complexes, sensations and emotions of the child; and thereby to act on the functions of the various organs through their close relationship to the psyche. It is superfluous to emphasize the necessity of an exact physical examination, so as not to overlook a somatic disease.

Disturbances of an imitative or induction origin will urgently necessitate the elimination of the inducing person or the removal of the child from his former obnoxious environment; otherwise, when this is impossible, one must not be surprised by recurrences. Yet, even then, permanent disappearance of the symptom in a number of instances were obtained, if the parents carried out the instruction not to make an exhibit of their own affections and by permanent complaining and mention of their own ailments to accentuate the baneful influence on the impressionable child. Czerny proposed for children suffering from pertussis, not to be kept in the same room, since the paroxysm in the one patient will often provoke an attack in the other.

In many cases, the intentional neglect of the child's morbid manifestations will have its important place; especially in irritative conditions, or when previously too great solicitude on the part of the environment, fostered and nurtured as mentioned before, the psychic fixation of the ailment and kept it permanently alive in the mind of the patient. The child may be directly told that his trouble is a minor one, that he exaggerates, or no word may be dropped in his presence, the ailment apparently disregarded and the child observed only without his knowledge. Many a symptom will thus be suppressed in the start. Cessation of the psychogenic complex will spontaneously ensue within a short time, once the child finds no more his sympathetic and interested "public." "The symptoms will gradually die of ennui. The child forgets them, so to speak, altogether" (Bruns).

A pathologic psychic reflex, occurring habitually, may be abolished either by not allowing the provoking "memories" to appear or by linking them up with new displacing associations; thus the unfolding of the former habitual associations—those in the waking state as well as those occurring during sleep—will be frustrated and entirely dislodged. Such memories are especially likely to fail to appear or to be entirely dislodged, if the child's entire life is radically altered, namely, by a complete change of its environment, as for instance by separation from the accustomed surroundings, the removal from the paternal home to a hospital. In other cases the change of the personnel, the introduction of a new attendant or sober-minded nurse will suffice to dislodge the morbid complex.

It is true, an alteration of the milieu in outspoken, hysterical children must be radical and comprise not only a change of place, but in addition, also the absence of visitors, especially the separation from family members, the leaving at home of toys and books or other objects that have been in frequent use by the child and therefore are closely connected and interwoven with his manifold associations and morbid complexes of ideas and emotions.

These facts give us the explanation, why we encounter so rarely in hospital practice disorders like somnambulism, pavor nocturnus and other allied oneirogenic disturbances, for evidently the children go to bed with entirely different ideas and thoughts than before, and the previous habitual or stereotypical dream-ideas with their psychomotor reactions do not come into existence.

It is worth recalling to mind the interesting fact, as Friedjung has emphasized, that sleep disorders not of oneirogenic origin, as difficulty in falling asleep, interruption of sleep and wakefulness of children in the night, with restlessness, asking questions and fitful desires and other evil sleep habits may also in most instances be corrected by such simple means as change of the bedroom. A slight change in the arrangements of the life of the child immediately before bedtime will likewise have its effect.

It will often have a most salutary effect for the child to meet and play with healthy and vigorous children; this will more than anything else divert his attention from his physical condition and, indeed, the imitative instinct of the neuropath by being directed into other channels will thus be utilized in bringing the child back to normal habits and tendencies.

Effectual and powerful as the change of milieu may be, circumstances will not always render it expedient, feasible or necessary. We will have to resort to other methods, all aiming likewise at diverting the child from his disturbances and altering favorably his entire conceptions, ideas, deductions and imaginations, conscious as well as subconscious.

Psychotherapy will here have to be addressed directly to the child through simple verbal suggestions, particularly with the support of appropriate apparatuses, auxiliary manipulations, as massage, medication or other supplementary physical means, that impress themselves on the child's mind as wonderful, mysterious or novel, and mask the psychic element of the treatment. The influence of suggestion may reach even the sphere of oneirogenic phenomena and other sleep anomalies, as has been mentioned before.

The certainty, often the rapidity, of a cure may be surprising to the observer, as the mere authoritative word, the emphatic and positive assurance of cure, or, according to the individuality of the patient, kind persuasion, encouragement and tact, reward or punishment, will remove the disturbance, the medicine administered serving merely — so to speak — as the "visible symbol and token of the invisible force." The authoritative, determined appearance of the physician, his "personality," the firm confidence of the little patient and his belief in the physician and his orders are the *conditio sine qua non* of a successful treatment of purely psychogenic ailments. Polypragmasy must be avoided. It is the How of administration more important than the What.

It would be preposterous and destructive of the physician's purpose, unwarrantedly to designate these "neurotic" disturbances as hysteria to the parents, who not infrequently resentfully would assail the physician's diagnostic acumen for this terminology, that is so utterly unpopular among laymen.

There is, of course, nothing novel in the principle of these methods, and psychotherapy has been practiced successfully from the beginning of empirical medicine, remaining throughout the ages inseparably connected with our art of healing. However, it was not only then that the disciples of the hippocratean art were unaware of the great therapeutic import of the psychic forces that their words, orders and prescriptions carried; that they scarcely suspected the paramount rôle psychic elements play in the composite aspect of the clinical pictures. They hardly could realize the true and real nature of the curative agency and principle. Wherever an adequate appreciation and appraisal of the psychic moments is still wanting, self-deception is likely to follow and without criticism to attribute too much merit to pharmaceutical preparations; this will lead to a regrettable neglect of a therapeutic principle that in systematic and rational application is bound to yield excellent results, far better than in the hand of the merely intuitive user among our profession, not to speak of the commercial faith healers, Christian scientists and other false prophets without any medical training, but with much pretension and arrogance.

I often found it good procedure to hold out and reiterate the prospect of cure not directly to the child, but in his presence to his mother, or in my dispensary work, in addressing the students, augmenting thereby the suggestive effect by the prestige and authoritativeness of the teacher.

By force of verbal suggestion, aided by pharmacodynamically often indifferent medicines, I succeeded in perhaps every case in abolishing the disorders, as tremor, pains, arthralgias, nervous dyspneas, palpitation of the heart, nervous vomiting, limping, etc. Naturally, one must be rather sure of being master of the situation; otherwise, if the first psychic blow falls very short of its goal and the prediction fails of early realization, the child's trust and faith in the curative force is considerably shaken and the probabilities of a cure by the same physician reduced. In cases of palsy it is often important to prove to the child that he can use his limbs much better than he supposed.

As a last resort — if not used at the first — a more powerful means, impressive through a certain degree of unpleasantness or even painfulness, will find its proper place; as for instance, the faradic current that even in tics, an usually obstinate affection, has proved to be of great curative value. Also cold baths, subcutaneous injections, bitter or disagreeable medicines and other measures of a disagreeable character come here into consideration.

In many instances a method that takes the patient by surprise by its sudden, unexpected application, as for instance, the faradic brush, cold douche, forcible extension of a contracted joint, especially in a changed environment, in the absence of the parents, be it only the office of the physician, finds its indication, particularly in cases of paralysis, contracture, aphonia, etc., or when the intentional neglect failed to create improvement. A strong faradic brush is, in fact, the most persuasive master in such cases. Before the mind of the child, confronting a strange personality and surrounded by a new environment, has had time to find its orientation, or before doubt and criticism could arise, the child overwhelmed at once must have surrendered and the result be obtained. The failure to subjugate the child under the force of suggestion will disclose to him "that he has not yet found his master," and the chances of cure are much diminished. According to the individuality of the child, a peremptory command, if necessary a severe word, may suffice. "The physician lifts up the paralyzed arm and letting it loose, briefly commands: Now keep the arm up" (Bruns).

It will most often be better and safer, instead of using the surprise method, to proceed gradually and slowly; we thereby aim not at the immediate and total, but only at the partial removal of the symptom by our verbal suggestion and encouragement, until within a few days the complete elimination is obtained. Especially may this method be necessary in cases of more severe disturbances in older children, in whom according to the patient's personality the attempt at a complete cure by one stroke might arouse the critical doubt, especially when manifold futile therapeutic measures have already been employed. Of course under all circumstances, any countersuggestive influence, as for instance, the expression of doubt as to the curability by surrounding persons, a careless remark or the aspect of a sick neuropathic individual must be avoided. It will be left to the physician's experience, ingenuity, discretion and sagacity to decide the kind of procedure in the individual case.

HISTORY OF A CASE OF ASTASIA AND ABASIA

G. K., a girl, aged 11 years, eight days before admission to the Cook County Hospital while retiring felt suddenly that her left leg became weak and gave way and she fell over into her bed. Since then she was bedridden and unable to stand or walk without assistance, dropping forthwith to the floor if not held up. At my first examination, the child's ability while in bed to move the lower extremities with energy, was deliberately dwelt on and suggestively emphasized in the presence of other physicians, as a very good sign of a speedy recovery. She took this as a proof that "her limbs were much better than she had thought." The next day she was able to walk a few steps unsupported, and with encouragement she became, on the third day, able to participate in the plays and running games of the children. No medication.

Psychotherapy is successfully applicable not only in purely and entirely psychogenic diseases, but also for the removal of psychogenic complexes that aggravate or complicate acute and chronic diseases of organic nature, and for the removal of psychogenic residues. They may be very insignificant or in other instances, by their intensity and duration, may far surpass the originally organic symptom, as for instance, the hysterical painful contractures of joints, or abasia and astasia. The recognition of the psychogenic nature of a disturbance by suggesting a possible neuropathic constitution will lead to a therapy that considers the entire individual and treats not merely the symptom, but the patient, employing in addition to the special treatment general measures which have an invigorating effect on the nervous system. It will lead to a pedagogical consideration of the problem and the employment of educational methods that aim at "psychic hardening." The child, too often spoiled, must learn to control his emotions and, subordinating himself to the educator, acquire the inhibitory influences of a well directed will power.

COMMENT

Psychotherapy in childhood particularly gains additional importance in consideration of its applicability as a differential-diagnostic medium in the distinction between neurotico-functional and organic disturbances. Its use, *cum grano salis,* with the point in view of confirming our diagnostic presumption, cannot be overestimated, and its instrumentality is ever emphasized in my teaching at the dispensary. An abundant material for the demonstration of such neurotic cases and their treatment aided substantially in bearing out these claims. A purely psychogenic symptom or residue of an organic disease will with a great degree of certainty be pronouncedly influenced, mostly very soon cured, or the psychogenic complication from the organic ailment so to speak subtracted, and thus our diagnostic endeavor aided. The diagnostic significance of a striking positive result in an obscure and questionable case, the diagnosis *ex juvantibus* rivals the differential diagnostic value of an effective mercurial cure in lesions suspicious of syphilis.

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HEAD SHAKING WITH NYSTAGMUS IN INFANTS

A STUDY OF SIXTY-FOUR CASES *

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Nomenclature.—Various names have been given to this condition. Those which include the word spasm, such as spasmus nutans, nutatio capitis spastica, gyrospasm, nodding spasm, are objectionable, because it is not a spasm in the sense in which that term is usually used. The terms gyrospasm, rotatory spasm, head nodding and nodding spasm are inaccurate, because the movements may be in any direction. The term spasmus nutans has sometimes led to confusion with the condition known as eclampsia or epilepsia nutans, which is an entirely different disease. Salaam tic, a term sometimes used by French authors, is objectionable because this condition has none of the characteristic features of a tic. Everything considered, head shaking with nystagmus, seems to be the least objectionable name.

Historical.—This condition was first described by Ebert[1] in 1850, and in 1851 by Romberg and Henoch.[2] In 1890 Hadden[3] published two important papers, with a report of twenty-one cases. Caillé[4] of New York was the first to note that when the nystagmatic eye or eyes were bandaged, the movements of the head ceased. In 1897 Raudnitz[5] published his exhaustive monograph on the subject, based on fifteen cases, in which he particularly emphasized the importance of the dark room in the etiology of this condition. In 1911 he published a report on the production of this condition experimentally in young dogs. In England and Scotland, Still[6] and Thomson[7] have reported large series of cases. In this country Peterson,[8] Aldrich,[9] Abt,[10] Judson,[11] Miller,[12] Hamill and Posey,[13] Hill[14] and others have published cases.

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Frequency.—This condition seems to be more common in some countries than in others, if we may judge by the number of reported cases. It is certainly more frequent in large cities. In Budapest at the children's clinic, 15 cases were observed in 3 years among 52,215 patients; in Prague, 8 cases in 2 years among 1,223 patients; in Edinburgh, 35 cases in 11 years among 21,752 patients; in Basel, 2 cases among 6,154 patients; in Christiania 10 cases were seen at the children's clinic in 10 years. The disease appears to be not uncommon in London, Edinburgh, Berlin; and in this country in New York and Philadelphia. During the last 19 years I have had 64 cases under my observation at various children's clinics in New York. The first 15 were seen during 1899, 1900, 1901, at the Good Samaritan Dispensary, chiefly in the service of Dr. Koplik. These figures would indicate that this condition is met with in New York City in about 1 in every 700 infants coming for treatment. The number of cases varies markedly in different years. In 1901 I saw 8 cases; in 1906, 9 cases; in 1910, 13 cases, and in 1918, 7 cases; whereas in some years, 1904, 1908, 1909, 1912, 1914, 1916, no cases were seen. This difference in the prevalence of the disease in different years has also occurred in other cities; for example, in Budapest, in 1891, there was one case in 17,400 patients; in 1894, 9 cases in 16,563 patients. It is relatively somewhat more common among negro children than among white children in New York. In 1910 I saw 10 cases in negro children at the Vanderbilt Clinic. This is probably due to the poor hygienic conditions and the greater prevalence of marked rickets in these children.

Sex.—Females are slightly more frequently affected. In my series, there were 29 males, 35 females. In 133 previously reported cases there were 62 males, and 71 females.

Seasonal incidence.—This condition shows a very distinct seasonal incidence, as shown in the accompanying tabulation.

OCCURRENCE OF HEAD SHAKING WITH NYSTAGMUS BY MONTHS

Previously Reported	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
110 cases	37	16	10	1	1	1	1	2	4	6	8	23
Herrman 64 cases	20	12	6	1	2	0	1	2	2	3	4	8
Hours sunlight Edinburgh (Thomson)	34	57	98	123	165	157	138	145	104	83	47	24
Hours sunlight Average, 1911-1917 New York, Herrman	140	177	223	220	270	288	279	265	243	200	177	151
Mean temperature Average, 1911-1917 New York, Herrman	33.5	29.7	37.2	49.7	60.7	68.3	74.7	72.9	66.4	57.1	44.7	34.4

It will be seen, Figure 1, that it is much more prevalent during the winter months, nearly 70 per cent. of all cases occurring during December, January, and February. The largest number of these begin in January, and recurrences are almost always in this month. As

Thomson has pointed out, the number of hours of sunlight, in temperate climates, is at its minimum during the winter months, Figure 2, and this may bear a definite relation to the prevalence of the condition. It may also account for the very few cases reported in France, Italy, and Spain, for it seems very unlikely that the disease could be overlooked. However, it does not appear probable that the relation is a direct one, and there is no reason to suppose that the amount of sunlight bears a direct relation to this disease. It would be interesting to determine whether head shaking is rare in countries in which there is an unusually large percentage of sunshiny days, for example, New Zealand, and whether the condition is prevalent in the months of December, January, and February in places in which the summer and winter seasons are different than our own. It will be noted, Figure 2, that the incidence curve of head shaking also corresponds quite closely to the mean temperature curve, so that the temperature might also be important, in so far as during very cold weather the windows would be closed and the infants would not be taken out as much as usual. This may possibly account for the unusually large number of cases seen during the past winter, which was an extremely severe one.

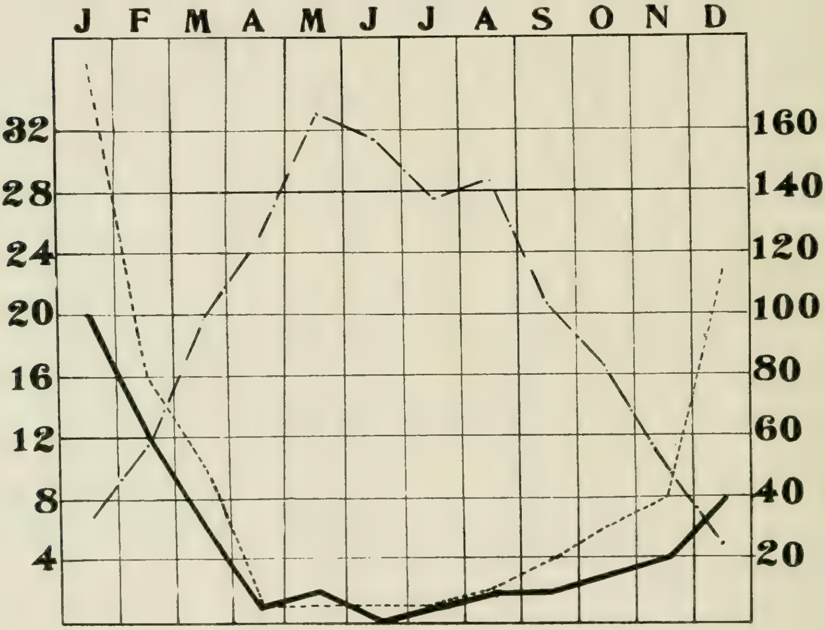

Fig. 1.—Seasonal incidence of head shaking with nystagmus; ———— sixty-four cases observed by the author; — — — — — — 110 previously reported; —.—.—. number of hours of sunlight each month in Edinburgh (Thomson).

Age incidence.—The disease is most common between 4 and 12 months of age, 75 per cent. of all cases occurring at that time. In my series the age of onset could be definitely determined in 61. It was 1 at 1 month, 2 at 2 months, 2 at 3 months, 2 at 4 months, 3 at 5 months, 8 at 6 months, 8 at 7 months, 5 at 8 months, 5 at 9 months, 6 at 10 months, 4 at 11 months, 6 at 12 months, 2 at 13 months, 3 at 15 months, 1 at 20 months, 2 at 21 months, and 1 at 4 years. The youngest in the series was 1 month old. Schoenberg[15] has also reported a case at that age, and Gee[16] one at 6 weeks of age. After the eighteenth month a first attack is rare, but there may be recurrences at that time. In some of the late cases, the original attack may have been overlooked. My oldest patient was 4 years of age. Henoch reported a case of 3 years, Still one of 4 years, and Mowat[17] one of 5 years. It is pretty well established that head shaking is a developmental disease, and that it occurs in certain predisposed infants at a time when the associated movements of the head and eyes are being perfected.

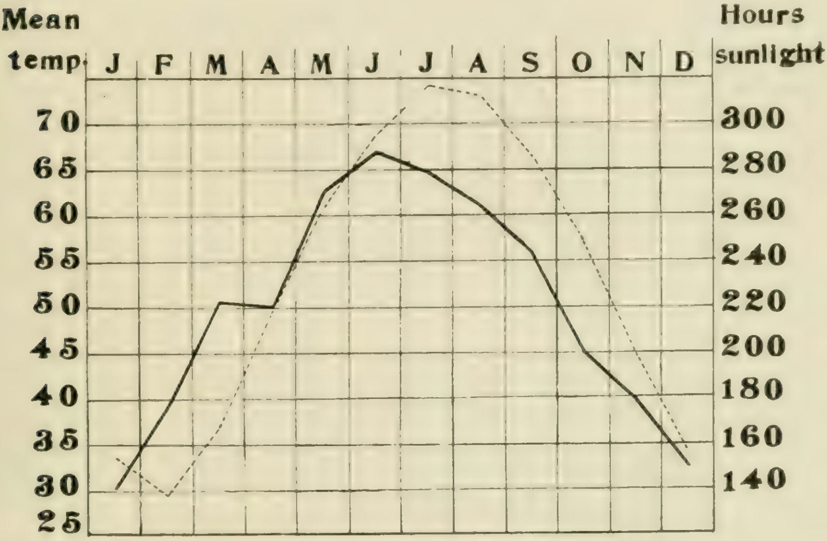

Fig. 2.—New York City, 1911-1917; ———— number of hours of sunlight; — — — — — mean temperature.

Family history.—In very few of my series, was there a distinct neuropathic family history. In 2 instances the parents were cousins. In 4 cases the mother was extremely nervous, in 3 markedly anemic;

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[15] Schoenberg: Norsk Mag. f. Lægevidensk., 1891, p. 467.

[16] Gee: St. Barthol. Hosp. Rep., 1886, **22,** 96.

[17] Mowat: Lancet, London, 1906, **2,** 397.

1 had frequent attacks of migraine; 1 had hysteria. In 5 families one or more of the other children had convulsions; in 1 family one child had epilepsy, and in another family a child died of meningitis. In one instance the condition occurred in twins, and in another family two children were affected. Henoch and Reyher also observed the disease in twins; and Thomson and Hadden have reported instances of more than one case in a family. Three of my cases occurred in mongolian imbeciles. Unlike the latter disease, head shaking does not attack more frequently the first or last child, and it is not more common in families in which there are a large number of children.

Previous history.—In three of my series, the labor was difficult and the delivery instrumental; one was a "twilight" baby, and one was prematurely born. None of these factors seem to play a part in the causation of head shaking.

Feeding.—At the onset of the disease, thirty-five of my patients were breast fed, eighteen artificially fed, and eleven were on mixed feeding, so that the character of feeding has no direct relation to the disease. As one would expect, the rachitic manifestations when present, were more marked in the artificially fed infants, so that to a certain extent such infants were somewhat more predisposed to head shaking.

Previous disease.—Illness, by lowering the vitality, apparently is an etiologic factor in those infants who are already predisposed. Five of my cases followed an attack of bronchitis, 3 followed pneumonia, 6 patients had digestive disturbances, 2 measles, and 1 each nasopharyngitis and otitis. Intercurrent disease tends to increase the head and eye movements.

Teething.—It is to be expected that this condition, which plays such an important etiologic rôle in the minds of mothers, should also be held responsible for head shaking. It would not be surprising if the nystagmus were ascribed to the eruption of the "eye" teeth. Ebert, Henoch, and Still, believe that the eruption of teeth often plays an important part as a source of peripheral irritation. In exceptional cases this may be so, but I have not been able to convince myself that the rôle is an important one. In 18 of my cases the onset of the disease antedated the eruption of teeth. Ebert, who first described the condition, writing in 1850, says, "It is well known that febrile and spastic conditions which are related to the eruption of teeth may antedate the actual appearance of the teeth." If we accept this statement, then anything is possible. I recently saw an infant in whom the eruption of two incisors occurred on the day on which a measles eruption appeared. To the lay mind it seems like cause and effect. In my patients teeth appeared during the course of the disease, but

I never noticed an exacerbation of the symptoms at that time. *Fatigue* does tend to increase the symptoms, so that it is possible that a fretful child that is teething may sleep less, and in that way the head movements might become more distinct. Other sources of peripheral irritation, worms, otitis, etc., have been mentioned as causes, but the evidence is not conclusive.

Trauma. Fall.—In a small percentage of cases this may reasonably be considered an exciting cause in a predisposed child; but it must be remembered that a large number of infants fall and very few show any permanent injury. Only when the head shaking begins shortly after the fall can a relation be claimed; and it is also possible that the fall is a symptom of an already existing coordination neurosis rather than its cause. In six of my series there was a definite history of a fall just preceding the onset of the disease. In one of Hadden's patients two relapses occurred following falls on the head. Peterson[8] says: "Perhaps a concussion of some kind may be found in most of the cases to be the determining factor—a concussion setting up in the centers of the spinal accessory and at times in those of the oculomotor nerves an arrhythmic discharge."

Hygienic conditions, social position, location of rooms.—The hygienic conditions and social position of the family play an important part. Many authors say that the disease does not occur among the well-to-do. This is not absolutely correct, as I have had two cases in families in comfortable circumstances, and Still mentions having seen three such cases. It is rare, however, among this class compared with the frequency with which rickets, laryngismus stridulus, tetany and convulsions occur in them. In large cities, head shaking is more common among those who live in the poorer tenement districts. In my series 11 families lived in the basement, 20 on the first floor, 9 on the second floor, 12 on the third floor, 7 on the fourth floor, and 5 on the fifth or top floor. It will be noted that one half of the families lived in the basement or on the first floor; those living in the basement were not only the poorest, but their rooms were dark and ill ventilated, and the intelligence of the mothers was lower than the average.

Dark rooms.—In 55 of the cases of my series the character of the rooms could be accurately ascertained. I visited nearly all of them myself. It is important to investigate oneself and to determine the exact conditions during the months preceding the onset of the disease. The crib may be placed in a dark corner of a room, not otherwise very dark; the shades may be drawn down a large part of the day so as to darken the room and favor sleep, or the crib may be curtained in order to prevent the light from shining in the infant's eyes. In 40 of my series, the infant was more or less in the dark, and in a large number of these cases it was necessary to use artificial light in the afternoon during the winter months. In the remaining 15 the room and the spot where the infant lay were fairly light, and in a few of these the room was bright even during the winter months. In several cases, although there was a light room, the infant was kept most of the time in the kitchen, a dark room, so that the mother could watch it while cooking; in several others it was impossible for the mother to take the baby out on account of sickness or the large number of other small children that required attention. On the other hand, in a few cases the mother definitely said that the baby was taken out regularly. It must be remembered that in certain crowded sections of the city a large number of people live in dark rooms, so that only a small portion, probably not more than 1 in 100 infants living in such rooms, contract the disease. Here again we must assume an individual predisposition. The same has been noted in so-called miner's nystagmus; only 3.5 to 4 per cent. of all coal miners working under exactly the same conditions are affected. There can be little doubt that the dark room is an important factor in a large number of the cases of head shaking. During the last eleven years I have seen the same class of patients at the Lebanon Hospital outpatient department in the Borough of the Bronx as I saw during 1899-1902 at the Good Samaritan Dispensary on the Lower East Side of New York. Making due allowance for the difference in the number of patients, the disease was more common in the latter section, principally, I believe, because in the Borough of the Bronx the majority live in rooms which are better lighted and better ventilated. A series of 4 cases of head shaking reported by Rietschel[18] from Finkelstein's service is interesting. On account of the suspicion of communicable disease these 4 infants were transferred from the well lighted ward of the infant asylum to the dark room of a barracks. Shortly after, they developed head shaking. One of the infants was returned to the well lighted and well ventilated ward of the asylum and the head movements soon disappeared. Raudnitz was able to produce experimentally a similar head shaking with nystagmus in puppies by placing them in a dark cage at or very shortly after birth. In from six to eight weeks they developed nystagmus, and after three or four months, shaking of the head. If they were placed in a darkened cage *after* they were 2 months old, these symptoms did not develop. Here again we note, that the causative factors act only at a certain stage in the development of the nervous mechanism which controls the associated movements of the head and eyes. As in infants, at first the nystagmus was only seen when the animal looked in certain directions or when the head was held, and the head movements ceased when the eyes were bandaged. If the animals were placed in the open a few days after the nystagmus first showed itself, it disappeared in from one to two weeks, and if they were returned to the dark cage, the nystagmus reappeared in from two to seven days. If the animal was kept in the dark, however, so that the nystagmus persisted for several months, it required as much as nine months' exposure to daylight to cause the nystagmus to disappear. The examination of the fundus, the vision, and the microscopic examination of the brain and retina of the affected animals showed no pathologic changes. It is worth noting that in Raudnitz' experimental work on animals the cage was dark and apparently there was no artificial light to which the eyes of these young animals was attracted. In explaining the causation of the condition in infants he laid stress on the straining of the eyes in looking at an artificial light some distance above the level of the head. Raudnitz believes that the nystagmus associated with the head shaking in infants is analogous to that observed in coal miners.[19] Although there are some points of analogy, there are some objections to this theory. The nystagmus of coal miners seems to be due to the strained position of the head, eyes, and body of the men, working in a place which is imperfectly lighted. The darkness alone is not sufficient, for this form of nystagmus occurs *only* in *coal* miners. The strained position of the head and eyes alone is not sufficient, for it does not occur in ceiling painters, and in others who have to look more or less constantly upward. A large percentage of the miners affected have errors of vision, while the infants with head shaking associated with nystagmus have no such error. The nystagmus of miners is usually bilateral and conjugate; that of the infants is usually unilateral, or is much more marked in one eye, and is frequently not conjugate. In miners head movements are uncommon and are only present in severe cases; in infants head movements are the rule. In miners the head movements do not cease when the eyes are bandaged as they do in the infantile form.

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[18] Rietschel: Charité-Ann., 1906, **30**, 152. Rietschel refers to John Thomson of Edinburgh, as an American. We should be very glad to claim him.

Rickets.—Kassowitz,[20] Hochsinger[21] and Stamm[22] consider the head shaking of infants a rachitic manifestation. In my series, 45, or 70 per cent., of the patients showed some manifestations of this disease. This is about twice as frequent as in other infants brought for treatment. Thomson's figures are 94.2 per cent. rickets in the affected infants, 46.9 in other infants. Of course the percentage of rickets

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19. Nieden: Nystagmus der Bergleute. Wiesbaden, 1894.
20. Kassowitz: Vorles. u. Kinderk. im alter d. Zahnung, Vienna, 1892, p. 165.
21. Hochsinger: Verhandl. d. Gesellsch. f. Kinderh., 1897, **14,** 238.
22. Stamm: Arch. f. Kinderh., 1902, **32,** 259.

will vary according to the clientèle. For example, in New York City, rickets is much more common in negro children, so that it is not surprising that every one of my 10 cases of head shaking in negro children showed distinct rachitic changes.[23] However, in 19 of my cases rickets was not present, so that it cannot be an indispensable factor. Several other points indicated by Thomson are of interest. In head shaking, antirachitic treatment is not followed by the rapid improvement which we are accustomed to see in rickets. This has been my own experience and is contrary to that of Stamm, who noted distinct improvement in the head shaking *in a few weeks*. Cases of head shaking are rarely associated with laryngismus stridulus, facial irritability, tetany or convulsions. In my series, although many had marked rachitic manifestations, only 3 had laryngismus stridulus and facial irritability, and in Thomson's 35 cases only 2 had laryngismus stridulus and facial irritability. There does not seem to be a distinct relation between the frequency of laryngismus stridulus and head shaking in a given locality. In Vienna, Kassowitz in six years saw 370 cases of laryngismus stridulus, that is on the average 61 cases a year; in Edinburgh, Thomson in three years saw only 61 cases, that is, 20 a year. On the other hand, Kassowitz in eight years saw only 9 cases of head shaking; that is, about one a year, while Thomson saw 35 cases in eleven years; that is, 3 a year. If these conditions were due, as Kassowitz supposes, to the increased vascularity of the bones of the skull and the neighboring tissues, then we should expect that head shaking would be frequently present in rachitic infants with craniotabes; however, such is not the case. Rietschel tested the electrical reactions in 4 cases of head shaking, and 3 of the 4 gave normal reactions. While head shaking is rare in well-to-do families, rickets, laryngismus stridulus, tetany, and convulsions are not uncommon. As is well known, rickets involves not only the bones, muscles and ligaments, but the central nervous system as well, so that it is not surprising that a rachitic infant should be somewhat more predisposed to the development of a functional neurosis.

Pathogenesis.—Notwithstanding the great amount of investigation on this subject, the exact explanation of the disturbance of the nervous mechanism which results in the head and eye movements is still something of a puzzle. The solution requires the combined investigation of the pediatrist, neurologist, and ophthalmologist. Thomson says:

> The nervous mechanism whose function is at fault is evidently that which includes the semicircular canals in its circuit, and which regulates the coordination of the movements of the eyes with those of the head. Dr. Alex Bruce tells me that the nucleus of Deiters (one of the end nuclei of the vestibular

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[23] Herrman: Arch. Pediat., 1910, **27,** 370.

> nerve, lying at the lateral angle of the fourth ventricle) is in all probability the seat of the disturbance. He infers this from its connection with the oculomotor nuclei and with the anterior cornua of the cord.

Henoch had about the same in mind when he wrote:

> The frequent combination of head shaking with nystagmus is interesting, as it indicates that the nuclei of the spinal accessory and the upper spinal nerves which supply the affected muscles of the head and neck, are in close relation to those of the eye muscles.

The most satisfactory explanation of the pathogenesis of this condition is that originally suggested by Hadden and later modified and amplified by Mills[24] and Aldrich. Mills says:

> Hadden believes that the symptoms point to an instability of the motor centers above the nuclei in the spinal cord and fourth ventricle, and he would therefore attribute the disorder to a functional or other disturbance of the cerebral cortex. The child has acquired certain voluntary or purposive movements of the head and eyeballs, but these have not as yet become thoroughly organized and fixed in the psychomotor areas of the brain, hence a dissolution takes place because of the instability of the strained cortical centers to stand the work to which they have been too early subjected.

Aldrich amplifies this as follows:

> The writer in considering the pathology of these cases accepts as a fact the obvious relation of the head and eye movements, hence we have to consider an automatic head and eye movement in a child of unstable nerve development, and at an age in which the associations of those necessary movements are being educated and fixed in the psychomotor areas of the brain. Anyone that has observed the head and eye movements of the infant cannot have failed to mark the incoordinated attempts at associated movements of the head and eyes. The fibrous connection between the visual areas of the cerebral cortex and the fovea centralis that is necessary to perfect vision does not fully develop until after birth, and only gradually becomes medullated and fit for function. After this process is completed, which takes place only when the cortical cell has attained a degree of maturity that provides ample nutrition for its axis cylinder, then the structural and physiologic integrity of the central neuron is complete. During this time the same process of development in the peripheral neuron is going on with even greater rapidity, and we have the beginning of one of the most wonderful and mysterious processes of the nervous system—the communication between the central and peripheral neuron. . . . Binocular adjustment, judgment of fixed objects, spatial relations, including station, are acquired by the child as the medullation progresses. If this progress of medullary development of the nerve supply of the eyes is either interfered with by disturbance of nerve nutrition or rendered functionally imperfect through early acquired opacity of the refracting media, or by congenital absence of a place in the retina that has more acute and perfect vision than elsewhere (fovea centralis), or a congenital defect in the receptive center in the cortex, or an exhaustion of any of that delicate apparatus, then we are liable to get a rapid to and fro movement of the eyes—nystagmus.

Symptoms. Movements of the head.—The movement of the head is usually the first manifestation noticed by the mother, but in a certain number it may be preceded by a peculiar "cocking" of the head to one side. In some the nystagmus may precede the head movements but may not be noticed because it is present only when the child looks in certain directions, or when the head is held. The muscles chiefly affected are the sternocleidomastoid, the trapezius and the rectus capitis. The movements are regular and rhythmical and from 60 to 100 a minute. Usually they are not continuous, but come on at longer or shorter intervals. The direction is rarely purely horizontal, vertical or rotary, but when primarily horizontal, slightly upward to one side and downward to the other, the excursions often being greater to one side. If primarily vertical, it is rarely a pure nod forward and backward. The movement may be a combination of the horizontal and vertical, and they may be in different directions at different times. In my series the movements were primarily horizontal in 44, vertical in 12, rotary in 4, and horizontal or vertical at different times in 4. The movements are often more distinct when the child is angry or fatigued, and during an attack of some intercurrent disease. They cease when the child is lying down and in sleep. There is, however, an occasional exception to this rule; for example, in one of my cases, in which the movements were unusually frequent and well marked, they continued when the child was lying down, and Amberg[25] also mentions a case in which the movements continued during sleep. It was first noticed by Caillé, and later by Raudnitz, that the movements of the head ceased when the eyes were bandaged. It is not possible to test this in all patients, because some object so strongly that the movements of the head due to anger prevent the drawing of definite conclusions; but in 14 of my cases, I was able to corroborate this statement. The movements of the head are best seen when the infant is gazing in the distance and is not interested in any particular object. If an object is brought within a short distance, so that it is definitely fixed, the movements of the head cease.

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[24] Mills: Am. Textbook Dis. Child., Ed. 2, 1894, p. 712.

Movements of other parts of the body.—I have not observed movements of the extremities, such as described by Thomson, Still, and others, or of the trunk, as reported by Hadden. Ausch[26] noticed in one of his cases movements of the hands, as if the child was vexed. I have frequently seen such movements in infants who were entirely free from head shaking.

The peculiar position of the head.—(Fig. 3).—About one-half of these patients have a peculiar way of "cocking" the head to one side and looking out of the corners of the eyes. This may precede the head movements and may persist after these movements have ceased. In

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[25] Amberg: Arch. Pediat., 1901, **18,** 831.

[26] Ausch: Arch. f. Kinderh., 1900, **28,** 161.

75 per cent. of the infants in whom this "cocking" was present the head was inclined to the left. This is noteworthy in connection with the fact that in sixteen of the twenty-three cases in which the nystagmus was unilateral, the left eye was affected. Some of the patients have a habit of looking down with a coy expression; others throw the head back and look out of the partially closed lids.

Movements of the eyes.—The nystagmus may appear before, simultaneously with or after the head movements. It may persist after the head shaking has ceased. In 35 of my cases the nystagmus was bilateral, in 23 unilateral. Of the latter, 16 affected the left eye, 7 the right eye. Even when the nystagmus was bilateral, it was frequently more marked in one eye. In 6 cases the nystagmus was not seen when the patients were examined in the ordinary way, but it is known that in some cases the nystagmus is so slight that it can only be detected by an ophthalmoscopic examination. The direction of the nystagmus is often not purely horizontal, vertical or rotary; it may be different in the two eyes, or when the patient looks in different directions. In the 58 cases in my series in which nystagmus was present, it was primarily horizontal in 36, vertical in 6, and rotary in 15; in the remaining case it was impossible to determine the direction. The movements of the eye are much more rapid than those of the head, about 200 to 300 a minute. The nystagmus is increased by holding the head, and is more distinct when the child looks in certain directions, usually when it looks upward and to the right, when the right eye is affected, and upward and to the left, when the left eye is affected. It is also more distinct when the child fixes an object at a short distance, and when the eyes are converged. It is not present during sleep, as I was able to determine in several infants that I examined. When the nystagmus is bilateral it is not necessarily conjugate. According to Thomson,[7] it differs from other forms in that

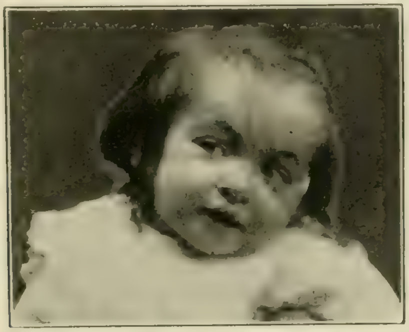

Fig. 3.—Peculiar cocking of the head seen in infants affected with head shaking with nystagmus.

the pupils alternately approach and recede. Spicer[27] was not able to verify this in all of his cases. Thomson also says that in rotary nystagmus the center of the pupil does not describe a circle, but an ellipse or an irregular figure. The movements of the head are not simply compensatory to those of the eyes, for the rate is different, and the two are not necessarily in the same direction; for example, the movements of the head may be vertical, while those of the eyes are horizontal. The nystagmus may persist after the head movements have ceased, and it may recur without the appearance of head movements. In exceptional cases the nystagmus may be the only manifestation. Such cases may be regarded as atypical or incomplete. In 4 of my series, convergent strabismus was present; in 3 there was hippus; 3 had associated movements of the upper lids, "nictitation;" and in 2 there was some sensitiveness to light; 12 of my patients were examined by ophthalmologists, and none of these showed any changes in the fundus, defects of vision or opacities in the media. Similar examinations reported by other authors were also negative, except that in two of Hadden's cases the fundus was light colored, and in one a slight crescent of atrophy was present around the left disk. In a few of my patients, I instilled homatropin in order to paralyze accommodation. The nystagmus was diminished, but the head movements continued. This is what one would expect, for as previously mentioned, the head movements cease when an object is distinctly seen and fixed; by paralyzing accommodation this becomes impossible. As nystagmus is sometimes associated with disturbances in the semicircular canals, Raudnitz had the ears examined in several cases. None showed any lesions, and syringing of the ears had no especial effect on the nystagmus.

Associated conditions. — In my series, 6 patients were anemic, 5 had an enlarged spleen, 2 tuberculous lesions, 2 papular urticaria, 2 eczema, 3 a geographical tongue, 1 blepharitis ciliaris. One child had attacks of apnea. Hadden reports cases with attacks of unconsciousness, partial or complete, and convulsions. Such cases are rare, and the more severe probably represent cases of so-called epilepsia nutans.

Duration.—The condition seldom lasts less than 2, or more than 12 months. In my series, the duration of 50 cases could be determined. In 6 it was 3 months; in 6 it was 4 months; in 12 it was 5 months; in 6 it was 6 months; in 4 it was 7 months; in 4 it was 8 months; in 2 it was 9 months; in 4 it was 10 months; in 6 it was 12 months. In 3 there was a recurrence during the following winter, 2 in January and 1 in February. In exceptional cases, however, the disease may last for more than one year. Spicer mentions a case in which it was present at 4½ years of age; and another in which the nystagmus persisted at 13 years of age.

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[27] Spicer: Brit. Med. Jour., 1901, **1**, 1120.

Subsequent history.—I have been able to follow 15 of my cases for a period of from two to ten years. Of these, 8 had no subsequent disease that had any relation to the head shaking. Of the remaining 7, 2 had enuresis, one of these until she was 6 years of age; 1 had convulsions; 1 pavor nocturnus; 1 a facial tic; 1 was extremely sensitive and also anemic; and 1 was a very restless sleeper and had grinding of the teeth. With the exception of the 3 cases in mongolian imbeciles, all the children showed a normal average mental development. I recently saw a girl of 13 years with a mild type of exophthalmic goiter (Graves' disease) who had had head shaking in infancy. In none of the 5 children who were followed to the eighth year did chorea develop. This is of some interest, as several authors have thought that there was a possible relation between these two diseases.

Diagnosis.—The principal features of this condition are so characteristic that the correct diagnosis is seldom difficult. Some of the earlier authors confused it with *eclampsia* or *epilepsia nutans*, which is really an epileptic equivalent. This disease occurs in attacks, and is associated with partial or complete unconsciousness. There is no nystagmus. In head shaking there are no sudden attacks, the movements are more or less continuous, and consciousness is not lost. The movements in head shaking are entirely different from those of a *tic* or *habit spasm*. They are smooth, regular, and rhythmical, not jerky. Tics do not occur at such an early age, and they are not associated with nystagmus. The *rocking* movements of the trunk and head, frequently seen in infants and young children, have only a remote resemblance to head shaking. The movements are voluntary, and even when they are not a manifestation of masturbation, seem to give the patients a certain amount of pleasure or satisfaction. Nystagmus is absent. Head shaking has occasionally been confused with the nocturnal movements of the head, *Jactatio capitis nosturnia,* which is sometimes seen in older children. These movements differ from the head shaking of infants in that they occur during sleep, or at least in a subconscious state, and are not associated with nystagmus. *Head rolling,* like head shaking, is seen in rachitic infants, but it is only present when the child is lying down; it is a voluntary act, and it is not associated with nystagmus. There is a rare form of *congenital head shaking with nystagmus* which is due to pathologic changes in certain areas of the brain. This condition as well as a number of other diseases of the central nervous system, associated with head movements or nystagmus, can easily be differentiated from the benign head shaking of infants, by the fact that the disease is progressive and persists throughout life. In all these conditions when nystagmus is present it is bilateral and conjugate.

Prognosis.—Head shaking with nystagmus in infants is a benign disease; all patients recover. The mothers may be assured that this disease will not interfere with the general health, or with the future mental and physical development of the child. The disease usually begins in the winter months and disappears during the following summer. Occasionally there is a recurrence of symptoms the following winter, but this also is of short duration. A few of the patients show a neuropathic tendency in later childhood.

Treatment. — The general condition, the hygienic surroundings, should be improved if possible. The room should be light, and the patient should be kept in the open air as much as possible. In several of my cases the mother noticed that there was a rapid improvement when the child was taken to the country. If there are any sources of peripheral irritation, these should be removed; if there are digestive disturbances, the diet should be regulated. Those infants that present rachitic manifestations should receive phosphorus and cod liver oil. In most cases this treatment is sufficient. I have not seen any marked improvement following the administration of bromids, belladonna or arsenic.

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THE EFFECT OF INJECTIONS OF PITUITARY SOLUTION ON THE URINARY OUTPUT IN A CASE OF DIABETES INSIPIDUS *

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The striking relief of symptoms in diabetes insipidus on injection of extracts of the posterior lobe and pars intermedia of the hypophysis cerebri has been known for some years, but no adequate explanation for the effect has yet been offered. Therefore, any new facts bearing on the action of pituitary solution should be made known.

A boy of 9½ years suffering from diabetes insipidus was studied in the St. Louis Children's Hospital in March, 1918. Attention is called to one of the results of this study. Injections of pituitary solution checked the rate of output of water and chlorids invariably; but checked the rate of output of urea, creatinin and uric acid little or none at all. The significance of this difference is not clear. Further study from this standpoint should be directed to other cases of diabetes insipidus, and to normal persons in whom artificial polyuria has been induced by the ingestion of large quantities of water; and to the other urinary constituents, in order to discover whether the excretion of electrolytes in general is hindered by the action of pituitary solution, while the excretion of nonelectrolytes in general is unaffected.

From a therapeutic standpoint, it may be said that this case showed the well known relief of symptoms when pituitary solution was given. There seemed to be no harmful effect from repeated injections, and it was considered practical to have this treatment continued at home.

REPORT OF CASE

M. G., a boy, aged 9½ years, was admitted to the St. Louis Children's Hospital, Feb. 23, 1918 (Case 12474), with a moderately severe case of diabetes insipidus and with the complaint that he drank lots of water and passed a large amount of urine.

Family History.—His father and mother were well. A brother of 11 years and a sister of 15 years were well. There have been no miscarriages and there was no history of tuberculosis in the family.

Past History.—The child was delivered spontaneously at term and was nursed one year. He had measles and pneumonia at 11 months. His tonsils and adenoids were removed at 6 years. He has had a divergent squint since birth and is very bright at school.

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* Submitted for publication July 17, 1918.

* From the Department of Pediatrics, Washington University Medical School, St. Louis, Mo.

Present Illness.—This began in August, 1917, with great thirst and copious urine. He is said to have passed 12 quarts a day. Has lost some weight and become pale and weak lately. His sleep has been disturbed by the pollakiuria. No other symptoms have been noted. Treatment so far has not helped him.

Physical Examination.—He was a well developed, bright boy of perfectly normal appearance, excepting for an external strabismus. The viscera were normal and there were no signs of endocrine disorder. The neurologic examination was negative, including the ophthalmoscopic examination. Pulse and temperature were normal.

Laboratory Examinations.—Blood: red blood cells, 4,566,000; white blood cells, 9,600; polymorphonuclears, 68 per cent.; hemoglobin (Sahli), 75 per cent.; urea nitrogen, 10.4 mg. per 100; normal protein nitrogen, 32.7 mg. per 100; plasma sodium chlorid, 0.625 per cent.; plasma carbon dioxid, 49.8 volume per cent. Wassermann reaction negative.

Phenolsulphonephthalein excretion: 52 per cent. first hour, 19 per cent. second hour; two hours, 71 per cent.

Lumbar puncture: Clear spinal fluid under no increase of pressure, 5 cells per cubic millimeter. Globulin test negative (Noguchi); Wassermann test negative.

Complement fixation test for tuberculosis was positive in serum; the von Pirquet test was slightly positive. Roentgenogram of the chest was negative. No signs of tuberculosis were discovered. Roentgenogram of the skull revealed slight convolutional atrophy; sella turcica normal.

Urine: Pale, from 6 to 7 liters per day, specific gravity from 1.001 to 1.003, no albumin, sugar, casts or cells.

EXPERIMENTAL

The patient was kept in bed for three days; for the remainder of the time, he was in a wheel chair during the day. His fluid intake was measured by the nurse in charge. On two occasions, he took water without permission. His diet was that given the other patients excepting that he had "salt-free" articles, March 2 and 3; and a specially prescribed and weighed diet, March 14 and 17.

Urine was collected in quart bottles from 6 a. m. to 6 a. m., and preserved under toluene in the refrigerator. The analytic methods were as follows:

Urea was determined by Marshall's method.[1] *Chlorids* were determined by Van Slyke and McLain's method, and expressed as "sodium chlorid."[2] *Creatinin* was determined by Folin's method.[3] *Uric acid* was determined by Folin's method.[4] *Calcium* was determined by Lyman's method.[5] *The acidity* was determined by titrating the diluted urine (usually diluted 1:10) with fiftieth-normal hydrochloric acid or sodium hydroxid, for neutrality with phenolsulphonephthalein as indicator. The results are expressed in cubic centimeters of tenth-normal acid or alkali. This method, of course, gives relative values only.

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[1] Marshall, E. K.: Jour. Biol. Chem. 1912-1913, **14,** 283.

[2] Van Slyke, D. D., and McLain, F. C.: Jour. Biol. Chem. 1915, **21,** 361.

[3] Benedict and Hitchcock: Jour. Biol. Chem., 1914, **17,** 469.

[4] Benedict and Hitchcock: Jour. Biol. Chem., 1915, **20,** 629.

[5] Lyman, H.: Jour. Biol. Chem., 1915, **21,** 551.

PITUITARY SOLUTION

The preparation known as surgical pituitrin was purchased from Parke, Davis and Company. It is said to possess about twice the activity of the obstetrical pituitrin. It represents the active constituents of the posterior lobe and pars intermedia of the pituitary glands of the ox. No disagreeable effects were produced on the patient, although he experienced a desire to defecate soon after the injections. No elevation in blood pressure followed the injections.

CLINICAL RESULTS OBTAINED

The effect of various procedures on the fluid intake and urinary output is shown in Table 1.

TABLE 1.—Summary of Daily Urine Volume in Case of Diabetes Insipidus Treated with Pituitrin

Date	Intake	Output			Pituitrin	Water
		Day	Night	Total		
2/27-28	2,450	1,714	940	2,654	....	Voluntarily limited
3/1-2	6,050	3,110	1,520	4,630	....	Not limited
3/2-3	6,750	3,565	2,835	6,400	....	Not limited
3/3-4	6,675	3,875	2,735	6,610	....	Not limited
3/4-5	2,825	2,106	450	2,556	0.5 c.c. hypodermically at 10:30 a.m.	Not limited
3/5-6	2,300	1,189	950	2,139	0.5 c.c. hypodermically at 7:30 a.m.	Not limited
3/6-7	2,650	1,667	470	2,137	0.5 c.c. hypodermically at 7:30 a.m.	Not limited
3/7-8	2,600	2,767	960	3,727	....	Not limited
3/8-9	1,273	870	910	1,782	1 c.c. hypodermically at 7:30 a.m.	Not limited
3/9-10	4,575	3,790	1,680	5,470	....	Not limited
3/10-11	3,000	3,720	2,000	5,720	1 c.c. by mouth at 10 a.m.	Not limited
3/11-12	3,585	3,747	2,000	5,747	2 c.c. by mouth at 10 a.m.	Not limited
3/12-13	1,950	1,303	370	1,673	0.25 c.c. hypodermically at 10 a.m. and 6 p.m.	Not limited
3/13-14	3,850	2,205	1,900	4,105	0.25 c.c. hypodermically at 8 a.m.	Forced in day
3/14-15	5,500	2,637	2,760	5,397	0.25 c.c. hypodermically at 9:45 a.m.	Forced in day
3/15-16	5,600	2,151	2,383	4,536	0.25 c.c. hypodermically at 10:45 a.m.	Forced in day
3/16-17	4,250	2,143	2,060	4,203	0.25 c.c. hypodermically at 10:30 a.m.	Forced in day

By strong voluntary effort, the patient succeeded in ingesting only 2,450 c.c. of water on February 27. His urine measured 2,654 c.c. This is much less than the intake and output on the next three days, when his fluid intake was not limited. A low salt diet did not diminish the output on March 2 and 3 and March 3 and 4.

On the morning of March 4, 0.5 c.c. of surgical pituitrin was injected subcutaneously in the region of the right deltoid. A very striking reduction of urine occurred. At the same time, thirst also diminished. The effects of pituitrin injections are similiar on the days following. It is especially to be noted that the patient's night urine was much lessened so that he awoke but once or twice to void.

On March 7, no pituitary solution kas given; the output rose to 3,727 c.c., or less than the usual level. This favorable effect of pituitary solution, persisting more than twenty-four hours, does not always occur, as is shown on March 9 and 10, when the output was 5,470 c.c., following the injection of 1 c.c. the day before.

TABLE 2.—Hourly Output of Urine on a Single Day as Influenced by 0.5 c.c. Pituitary Solution Injected at 10:45 a. m. Increase of Specific Gravity, and Decrease of Water and Chlorid Output

Time	Volume, C.c.	Specific Gravity	Urea Nitrogen		Sodium Chlorid	
			Per Cent.	Grams	Per Cent.	Grams
6- 7 a. m.	285	1.004	0.073	0.21	0.13	0.37
7- 8 a. m.	385	1.003	0.078	0.30	0.083	0.31
8- 9 a. m.	365	1.004	0.095	0.35	0.092	0.35
9-10 a. m.	310	1.004	0.089	0.27	0.10	0.31
10-11 a. m.	270	1.003	0.073	0.20	0.09	0.24
11-12 a. m.	24	1.012	0.708	0.17	0.15	0.036
12- 1 p. m.	36	1.009	0.63	0.23	0.19	0.069
1- 2 p. m.	49	1.011	0.35	0.17	0.17	0.083
2- 3 p. m.	74	1.011	0.56	0.41	0.17	0.128
3- 4 p. m.	104	1.010	0.05	0.05	0.17	0.18
4- 5 p. m.	104	1.009	0.31	0.32	0.19	0.20
5- 6 p. m.	100	1.009	0.017	0.02	0.24	0.23
Day	2,106	....	0.128	2.70	0.12	2.61
Night	450	1.010	0.14	2.80	0.076	0.34
Total	2,556	....	0.129	5.50	0.113	2.95

Given by mouth in this case, the pituitary solution was quite inactive up to doses of 2 c.c.

When pituitary solution was injected in two doses of 0.25 c.c. each, the effect was more striking than when given in a single dose of 0.5 c.c. This method of divided doses is more necessary in cases of greater severity than in such a case as the present one.

When the fluid intake is forced to a level about twice as great as the patient would choose, and pituitary solution is injected in the morning, the day output is somewhat lowered, while the night output rises to compensate for the intake.

More detailed studies of the effects of injections of pituitary solution are presented in the series of tables. Two hourly or one hourly specimens of urine were collected from 6 a. m. to 6 p. m., with a single night specimen, from 6 p. m. to 6 a. m. The injections were usually made about 9 or 10 a. m. In this way, one has two or four hourly specimens of urine before an injection, in order to establish a level of urinary excretion; and a fairly long period after the injection to observe its effects. No special effort was made to restrict the fluid intake.

TABLE 3.—Two-Hourly Output of Urine for Three Days; no Pituitary Solution Being Given. Variations in Urea and Chlorid Output. Total Output not Lessened by Low Salt and Nitrogen Diet

Time	Vol.	Urea N	NaCl	Vol.	Urea N	NaCl	Vol.	Urea N	NaCl
6- 8 a. m.	755	1.16	0.725	430	0.602	0.179	610	0.587	0.595
8-10 a. m.	530	0.89	0.579	520	0.388	0.156	670	0.556	0.506
10-12 a. m.	300	0.56	0.257	640	0.825	0.196	810	0.382	0.745
12- 2 p. m.	660	0.99	0.341	735	0.962	0.268	600	0.825	0.505
2- 4 p. m.	670	1.61	0.657	410	0.399	0.254	630	0.662	0.547
4- 6 p. m.	195	0.27	0.123	830	0.621	0.403	555	0.514	0.274
Day..........	3,110	5.48	2.68	3,565	3.80	1.46	3,875	3.53	3.17
Night.........	1,520	3.27	4.74	2,835	3.97	1.95	2,735	2.73	1.10
Total......	4,630	8.75	7.42	6,400	7.79	3.41	6,610	6.26	4.27
Date..........	March 1-2			March 2-3			March 3-4		
Diet..........	Regular			Low Salt			Low Salt		

Table 2 shows the result of injecting 0.5 c.c. of pituitary solution at 10:30 a. m., March 4. Before the injection the hourly output of urine is high, and fairly constant, of low fixed specific gravity and low sodium chlorid and urea concentration. Following the injection, there is, *within half an hour,* much more concentrated urine, of higher sodium chlorid and urea content, and of only about one-eleventh the volume per hour. The effect slowly disappears, but is evident throughout the remainder of the day.

When one considers the actual quantity of urea and chlorid excreted per hour, one sees a striking difference. Whereas, the actual amount of urea excreted per hour is only slightly affected by the injection of pituitary solution, the amount of chlorid excreted per hour is considerably reduced for several hours. On other days, Table 4, the suppression of chlorid excretion is always to be found; sometimes, but not as a rule, the urea excretion is also diminished. Irregularities of this sort may be dependent on other factors, such as food intake. The results of analyses made when no pituitary solution is given are shown in Table 3.

TABLE 4.—Hourly Output of Urine for Three Days as Influenced by Injections of Pituitary Solution

Time	Vol.	Urea N	NaCl	Creatinin	Vol.	Urea N	NaCl	Creatinin	Vol.	Urea N	NaCl	Creatinin	Uric Acid
6- 7 a.m.	285	0.207	0.366	21.1	145	0.257	0.381	29.0	262	0.411	0.697	52.0	62.4
7- 8 a.m.	385	0.302	0.314	23.5	132	0.081	0.359	17.0	182	0.238	0.495	17.8	48.3
8- 9 a.m.	365	0.347	0.349	23.2	20	0.010	0.049	8.8	37	0.167	0.079	15.4	41.0
9-10 a.m.	310	0.269	0.313	18.5	2	.....	.....	....	40	0.243	0.142	17.3	42.7
10-11 a.m.	270	0.197	0.243	14.7	70	0.102	0.244	28.0	54	0.382	0.210	23.7	54.6
11-12 a.m.	24	0.171	0.036	12.3	50	0.051	0.163	14.5	70	0.263	0.255	17.1	36.2
12- 1 p.m.	36	0.227	0.069	13.3	70	0.069	0.192	16.0	95	0.405	0.365	23.5	40.4
1- 2 p.m.	49	0.173	0.083	16.0	100	0.148	0.211	16.0	230	0.504	0.850	31.5	66.3
2- 3 p.m.	74	0.414	0.128	22.1	156	0.131	0.342	20.3	295	0.767	0.849	36.3	
3- 4 p.m.	104	0.052	0.176	29.2	158	0.160	0.321	19.0	2				
4- 5 p.m.	104	0.322	0.195	18.4	156	0.181	0.220	17.2	205	0.586	0.551	26.5	
5- 6 p.m.	100	0.017	0.232	23.8	130	0.086	0.143	16.9	195	0.727	0.622	29.6	
Day.......	2,106	2.70	2.50	227.0	1,189	1.28	2.63	203.0	1,667	4.70	5.12	291.0	
Night.....	450	2.80	3.42	167.0	950	1.39	1.76	172.0	470	1.26	1.80	159.0	
Total.....	2,556	5.50	5.92	394.0	2.139	2.67	4.39	375.0	2.137	5.96	6.92	450.0	
Date......	March 4-5				March 5-6				March 6-7				
Diet.......	Low Salt				Regular				Regular				
Pituitrin..	0.5 c.c. hypodermically at 10:45 a.m.				0.5 c.c. hypodermically at 8:45 a.m.				0.5 c.c. hypodermically at 8 a.m.				

It was thought that the rate of elimination of creatinin and uric acid might be less influenced by food ingestion than that of urea.

The output of these substances as influenced by the injection of pituitary solution is only moderately hindered (Table 4).

FURTHER OBSERVATIONS

In order to further study the effect of injections of pituitary solution on the output of water, salts, and nitrogen, the rates of intake of these substances were made practically constant. For three days the patient received a measured diet, which contained from 3.9 to 4.3 gm. of nitrogen and 2 gm. of sodium chlorid per day; he was induced to drink 150 c.c. of water every half hour from 6 a. m. to 6 p. m.

TABLE 5.—HOURLY OUTPUT OF URINE AS INFLUENCED BY PITUITARY SOLUTION WHEN WATER WAS FORCED—150 C.C. EVERY HALF HOUR FROM 6 A. M. TO 6 P. M., AND WHEN CHLORIDS WERE FORCED, 1 GM. EVERY HOUR FROM 6 A. M. TO 6 P. M.; 0.25 C.C. OF PITUITARY SOLUTION GIVEN AT 9:45 A. M.

Time	Vol.	Sp. Gr.	Urea N		NaCl		Creatinin		Uric Acid		Calcium	
			%	Gm.	%	Gm.	Mg.*	Mg.	Mg.*	Mg.	Mg.*	Mg.
6- 7 a.m.	345	1.005	0.085	0.29	0.25	0.86	7.2	24.8	4.6	16.0	2.8	9.8
7- 8 a.m.	370	1.004	0.074	0.27	0.19	0.70	6.9	25.3	5.1	19.0	2.8	11.0
8- 9 a.m.	330	1.005	0.078	0.26	0.20	0.65	7.2	24.1	5.0	17.0	3.6	12.0
9-10 a.m.	315	1.003	0.068	0.21	0.12	0.36	7.2	23.0	4.9	16.0	2.3	7.2
10-11 a.m.	165	1.017	0.27	0.04	0.45	0.07	47.6	7.9	3.3	5.4	1.3	2.1
11-12 a.m.	47	1.013	0.34	0.16	0.47	0.22	40.0	19.0	2.5	12.0	1.2	5.5
12- 1 p.m.	58	1.017	0.41	0.24	0.64	0.36	43.7	25.0	2.7	16.0	1.0	6.1
1- 2 p.m.	60	1.014	0.25	0.15	0.45	0.27	27.7	17.0	2.2	13.0	5.5	3.3
2- 3 p.m.	140	1.006	0.20	0.28	0.25	0.35	15.5	22.0	1.1	15.0	3.3	4.6
3- 4 p.m.	200	1.007	0.12	0.24	0.30	0.59	9.3	19.0	6.1	12.0	6.7	7.4
4- 5 p.m.	480	1.008	0.071	0.34	0.22	1.05	4.8	15.0	2.8	14.0	4.4	21.0
5- 6 p.m.	275	1.005	0.056	0.15	0.16	0.43	4.0	11.0	2.9	7.6	4.1	11.0
Day...........	2,637	...	0.10	2.63	0.22	5.91	8.8	23.3	6.2	163.0	3.8	101.0
Night....	2,760	....	0.058	1.60	0.22	6.07	8.3	230.0	5.4	150.0	4.8	133.0
Total.........	5,397	....	0.078	4.23	0.22	11.98	8.6	463.0	5.8	313.0	4.3	234.0

* Milligrams per 100 c.c.

On the first day, he received in addition, 1 gm. of sodium chlorid, given in water, every hour from 6 a. m. to 6 p. m. Pituitary solution, 0.25 c.c., was injected at 9:45 a. m. As before, the volume of urine is strikingly diminished for from 4 to 5 hours after the injection of the pituitary solution. The rate of salt output before injection is about 0.64 gm. per hour; for five hours after injection, it averages 0.25 gm. per hour. The rate of urea nitrogen excretion falls from 0.25 gm. per hour to 0.16 gm. per hour; creatinin, uric acid, and calcium show changes similiar to that of the urea nitrogen.

TABLE 6.—Hourly Output of Urine as Influenced by Pituitary Solution when Water was Forced—150 c.c. Every Half Hour from 6 a. m. to 6 p. m., and when Urea was Forced, 1.6 gm. Every Hour from 6 a. m. to 6 p. m.; 0.25 c.c. of Pituitary Solution Injected at 10:45 a. m.

Time	Vol.	Sp. Gr.	Urea N		NaCl		Creatinin		Uric Acid		Calcium		Acidity	
			%	Gm.	%	Gm.	Mg.*	Mg.	Mg.*	Mg.	Mg.*	Mg.	Per 100	Total
6- 7 a.m.	305	1.005	0.14	0.42	0.19	0.58	7.8	24	7.7	23	3.7	11.0		
7- 8 a.m.	330	1.004	0.15	0.49	0.17	0.56	6.9	23	7.4	25	2.4	8.2	1.2	3.9
8- 9 a.m.	195	1.005	0.20	0.38	0.10	0.20	8.3	16	10.0	20	2.7	5.3	3.3	6.4
9-10 a.m.	300	1.003	0.15	0.46	0.037	0.11	6.2	19	7.2	21	1.3	3.9	1.1	3.4
10-11 a.m.	205	1.004	0.23	0.46	0.056	0.12	15.0	30	11.0	23	1.6	3.3	1.9	3.9
11-12 a.m.	36	1.019	1.10	0.40	0.18	0.062	46.0	17	44.0	16	4.9	1.8	4.8	1.7
12- 1 p.m.	45	1.019	1.29	0.58	0.14	0.063	45.0	20	39.0	18	4.7	2.1	13.1	5.9
1- 2 p.m.	45	1.020	1.14	0.51	0.13	0.057	43.0	19	34.0	15	0.8	0.4	6.2	2.8
2- 3 p.m.	56	1.016	0.76	0.43	0.052	0.029	25.0	14	21.0	12	1.1	0.6	3.1	1.8
3- 4 p.m.	64	1.008	0.55	0.36	0.025	0.016	19.0	12	13.0	8.3	1.1	0.72	3.5	2.2
4- 5 p.m.	270	1.006	0.25	0.68	0.022	0.059	8.3	22	6.2	17	1.6	4.5	2.3	6.2
5- 6 p.m.	300	1.004	0.36	1.07	0.019	0.057	5.9	18	5.4	16	2.9	8.7	2.4	7.1
Day........	2,156	.....	0.29	6.27	0.089	1.91	10.9	234	10.0	214	2.3	50.5	2.4	45.0
Night......	2,385	1.001	0.23	5.41	0.028	0.68	9.3	220	6.3	150	2.9	69.0	2.4	58.0
Total.....	4,541	.....	0.26	11.68	0.061	2.79	10.0	454	8.1	364	2.6	119.5	2.3	103.0

* Milligrams per 100 c.c.

On the second day, 1.6 gm. of pure urea (0.75 gm. urea nitrogen) were given in water every hour from 6 a. m. to 6 p. m. The urea was eliminated at an almost constant rate of 0.44 gm. of urea nitrogen per hour. This rate is scarcely affected by the injection of pituitary solution. The chlorid elimination is large in the first hour and thereafter sinks rapidly. The phenomenon, observed also on the following day, is known as the "morning flush." The sinking is not greatly accelerated by pituitary solution, possibly because the level is already low. The creatinin and the uric acid output show little change; the calcium output is diminished.

On the third day, no urea or sodium chlorid was added to the diet. There is very little effect of pituitary solution on elimination of chlorid or urea, both these substances being present only in low concentrations in the urine.

Study was made of acid elimination by the urine on the last two days. The number of cubic centimeters of tenth normal sodium hydroxid required to neutralize the urine is indicated in the last column of the tables. On the third day 1 gm. of acid codium phosphate was given every hour from 6 a. m. to 6 p. m. As is seen, the "acidity" of the urine is much greater on this day. There is little if any diminution of acid elimination following the injection of pituitary solution.

TABLE 7.—HOURLY OUTPUT OF URINE AS INFLUENCED BY PITUITARY SOLUTION WHEN WATER WAS FORCED—150 C.C. EVERY HALF HOUR FROM 6 A. M. TO 6 P. M., AND WHEN ACID SODIUM PHOSPHATE WAS GIVEN, 1 GM. EVERY HOUR FROM 6 A. M. TO 6 P. M.; 0.25 C.C. PITUITARY SOLUTION INJECTED AT 10:30 A. M.

Time	Vol.	Sp. Gr.	Urea N		NaCl		Creatinin		Uric Acid		Calcium		Acidity	
			%	Gm.	%	Gm.	Mg.*	Mg.	Mg.*	Mg.	Mg.*	Mg.	Per 100	Total
6- 7 a.m.	670	1.001	0.12	0.83	0.083	0.56	7.4	50	7.6	50.0	5.4	36.0	2.4	16.0
7- 8 a.m.	280	1.003	0.081	0.23	0.085	0.24	8.6	24	7.3	20.0	4.0	11.0	3.2	8.9
8- 9 a.m.	100	1.002	0.11	0.17	0.040	0.064	12.0	18	8.8	14.0	5.3	8.5	11.0	17.0
9-10 a.m.	170	1.002	0.12	0.20	0.020	0.032	12.0	21	8.5	15.0	6.0	10.0	11.8	20.0
10-11 a.m.	65	1.006	0.16	0.10	0.031	0.031	23.0	15	16.0	10.0	8.0	5.0	27.0	18.0
11-12 a.m.	31	1.014	0.44	0.14	0.048	0.015	60.0	18	11.0	3.1	10.3	13.0	58.0	18.0
12- 1 p.m.	41	1.017	0.48	0.20	0.030	0.012	47.0	19	7.9	3.2	26.0	11.0	69.0	28.0
1- 2 p.m.	42	1.015	0.40	0.17	0.024	0.010	42.0	18	6.3	2.6			51.0	20.0
2- 3 p.m.	49	1.013	0.32	0.16	0.015	0.007	37.0	18	4.1	2.9			55.0	27.0
3- 4 p.m.	67	1.006	0.17	0.12	0.016	0.011	22.0	15	2.6	4.5			34.0	23.0
4- 5 p.m.	243	1.005	0.10	0.24	0.010	0.024	10.0	25	1.2	4.1			17.0	42.0
5- 6 p.m.	325	1.005	0.059	0.19	0.009	0.029	6.2	20	1.5	4.8			10.0	33.0
Day........	2,143	.....	0.13	2.75	0.049	1.04	12.2	261	6.2	133.0			12.3	271.0
Night......	2,060	1.003	0.063	1.30	0.011	0.22	8.9	183	1.9	39.0			1.2	246.0
Total......	4,203	.....	0.096	4.05	0.030	1.26	10.5	444	8.1	172.0			12.1	517.0

* Milligrams per 100 c.c.

Unfortunately, the patient left the hospital before further studies could be made.

SUMMARY

1. Study is made of the urinary output of a 9½ year old boy suffering from diabetes insipidus, as influenced by injections of pituitrin.

2. Following injections of from 0.25 to 1 c.c. of surgical pituitrin, there is a marked diminution of the urine volume.

3. This diminution persists for from 5 to 6 hours, sometimes much longer.

4. The volume of night urine is reduced when pituitrin is injected at any time on the preceding day.

5. The hourly rate of elimination of chlorids is always reduced after injections of pituitary solution.

6. The hourly rate of elimination of urea is usually only slightly, if at all, reduced by injection of pituitary solution.

7. The hourly rates of elimination of creatinin and uric acid are only slightly reduced by injection of pituitary solution.

8. The hourly rate of elimination of titratable acids in the urine is only slightly influenced by these injections.

9. The hourly rate of elimination of no substance studied is increased by injections of pituitary solution.

10. When the hourly ingestion of water and sodium chlorid or urea is maintained at a constant high level, the urea elimination is quite uninfluenced by the injection of pituitary solution, whereas, the chlorid elimination is considerably diminished, and the water elimination very much diminished.

11. Pituitrin injections in diabetes insipidus control urine output primarily and thirst secondarily.

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PUERICULTURE IN FRANCE*

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During the last quarter of a century scientific methods have replaced empiricism in the protection of pregnant women and of nurslings. A coordinated program was elaborated with ideas more and more distinct, and this program has been applied in more and more numerous instances, each day becoming more adequate.

In the establishment of this scientific plan it would be an injustice to misunderstand the secular participation of good sense and of tradition. In the eighteenth century Jean Jacques Rousseau recommended very forcefully maternal nursing as the ultimate solution.

HISTORICAL REVIEW

In conformity with these appeals to reason and sentiment, a memorable series of charitable initiatives followed, through the clairvoyant French Revolution, from St. Vincent de Paule to Théophile Roussel. The Queen, Marie Antoinette, in patronizing the Society for Material Charity had the vision of realities, as did Barère and Maignet, members of the "Convention."

The author of the "Contrat Social" demanded special privileges for pregnant woman; he preceded the accoucheurs, who, from Mauriceau to Tarnier and his followers, had been useful teachers and sure guides.

A complete history, with the indications of all the stages, would exceed the scope of this short study.

All these progressive improvements are intercorrelated. A famous discussion in the Academy of Medicine of Paris provoked the passage of the law of 1874 (Loi Roussel) for the protection of children placed in nursing homes. With the object of preventing the abandoning of children, infanticide and abortion, there were founded homes for pregnant women where they were able partially to support themselves during their pregnancy, together with allocations for pregnant women and asylums for postpartum convalescence.

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The progress of obstetrics and pediatrics has caused a salutary application of this law. Medical analysis as to the causes of infant mortality demonstrated the old necessity of pure sterilized milk, in the same manner as it has shown the deplorable results of the ignorance of mothers and wet-nurses.

With the object of instructing these women, Pierre Budin founded in 1892, the Consultation de Nourrisson, or Children's Clinics, which, at the same time, served to supervise the health of the infants.

At the same time, the system of the Goutte de Lait (that is to say, a baby clinic with the additional factor of supplying pure milk) was founded, and played a considerable rôle in controlling maternal nursing or mixed feeding.

ESTABLISHMENT OF REFUGES FOR WOMEN

The creation of "working refuges" for pregnant women was primarily in the interest of those illegitimately pregnant or those who were very poor, and demonstrated the necessity for a physiologic care during this period. Professor Pinard and others of his collaborators and students, Dr. Bonnaire among them, showed conclusively the value of repose previous to the accouchement from the point of view of the duration of gestation, and also of the weight of the new-born child.

Far-seeing philanthropy and useful science were in concord as to the advisability of placing on a firm and solid basis the doctrine of the protection of future mothers.

AIDS TO PROSPECTIVE MOTHERS

From 1877, the Swiss Confederation had promulgated legislation destined to regulate the industrial work of women during the prenatal period, as well as in the weeks immediately succeeding the confinement. The international conference in Berlin, in 1890, solemnly sounded the note of necessity in obliging repose during the period of maternal convalescence.

As early as 1846, a more or less cooperative organization in Mulhouse was founded among the work women, permitting them rest and an indemnity during their confinement. Similar organizations called Mutualités Maternelles were soon established in different regions of France under the patronage of Jules Simon with his collaborators Brylinski, Dalsace and F. Poussineau. A complete system of insurance in different countries has served as a basis for these parliamentary and regulatory measures, which, in order to be at the same time legitimate and effective, require concomitant aid. The choice of methods is of little importance so long as the ultimate object is attained. But the work of charity, in spite of its incontestible merits, has not the same moral value as this cooperation and insurance.

Each nation works with its institutions, adapting them to its own customs, and continually perfects them in order to secure the greatest benefit.

After long preparatory efforts, the French Government finally installed, in 1914, a definite system by which aid was furnished to mothers, inaugurated by the law of June 7, 1913, with some later modifications and extensions.

This recent legislation, from which hygienists expect the most happy results, does not only decree an elective, but an indemnified sojourn of repose before confinement and obligatory and indemnified rest after delivery; it requires also the sanitary control of nurslings in the homes, and it also makes appeal to private organizations—the Mutualités Maternelles, societies for mutual aid and societies for maternal assistance.

OBJECT OF RECENT LEGISLATION

This conjunction of efforts, in which industrial and commercial enterprises must participate, is made with the object of surrounding women's work, so extensive during the war, with a protecting shield.

It is indeed very important, and the legal institution of these "Chambres d'Allaitement" indicates this new line of thought — that when the mothers are obliged to work in the factories (especially for munitions during the war), this does not allow of the accomplishment of their family obligations, so essential at any time, but fundamental in the course of what is almost a crisis of natality of their country.

This far-seeing collaboration of private, mutual and philanthropic societies with the state, must not only content itself with the limitations of the law and restrictions of public assistance; it should be one of growing usefulness for the advancement and prolongation of its legal action.

VALUE OF EDUCATING FUTURE MOTHERS IN PROPER HYGIENE

From the beginning of the period of fertility in women, all the necessary precautions should be taken to educate them as future mothers, in order to instil into them the appropriate counsel, and to inculcate in them a spirit of security and confidence, as a result of which disastrous consequences may be avoided

Every movement must enter the combat against abortion, against overwork and against pauperism. The means vary; the end does not change. Working refuges, maternal canteens, aids to pregnant women, prenatal care, maternity homes, asylums for homeless children, rest-rooms after confinement, asylums for maternal convalescence, aids to nursing, the Mutualités Maternelles, the Consultation de Nourrisson, the Gouttes de Laite, *crèches,* Chambres d'Allaitement, *pouponnières,* temporary asylums for children, clothing supply stations, societies for maternal charity and for maternal nursing, protection of infancy — all these varieties of public endeavor, either private or public, are bound together, are complementary one to another, thus forming a compact and harmonious whole.

La Ligue Contre la Mortalité Infantile (that is, the league against infant mortality), without claiming any monopoly, endeavors to be a central organization for the stimulation of effort, always in collaboration and accord with the Ministry of the Interior.

CHANGES CAUSED BY THE WAR

The requirements of the great war have given birth to new institutions, as, for instance, the Office Central d'Assistance Maternelle et Infantile de Paris, which, created with the main fundamental ideas of the Ligue Contre la Mortalité Infantile and with other organizations, has been able to realize in the Parisian region, a permanent coooperation between the assistance *publique* and the private societies, whether new or old.

The military mobilization of physicians has retarded, and in some cases even paralyzed, in a great part of France, the work of propaganda undertaken before August, 1914; nor has it facilitated the application of the law to the assistance of the pregnant women.

The opportune and valuable cooperation of the American Red Cross will powerfully contribute to fill in the blank spaces and to overcome the delays.

AN IMPORTANT PROBLEM FOR FRANCE

No problem is more vital for the future of France than that of the determined and effective fight against depopulation with its many causes.

Experience and science demonstrate that the saving of the race depends on the saving of the seed; it teaches us that the national protectorate is not accomplished in a short period, but that it must be extended over an entire cycle — from the cradle to the school, from the school to the work-shop, from the work-shop to the regiment or the home; it must be present at the marriage, so that the young couple may be instructed and prepared for their duties.

In consequence, there will be an end to the separation of private and public societies, so that in all their activities, domestic and household preparation, together with maternal education, will not permit of blanks in this teaching.

An apprenticeship to bodily and personal hygiene naturally leads to household cleanliness. Social hygiene is not fragmentary; it is a block of which all its parts are interdependent.

Aids to mothers, protection of nurslings, safeguarding of children, in schools or as apprentices, the protective societies for young girls, support one another in contributing efficaciously, victoriously, to the combat against infant mortality, to that necessary and incessant battle against conditions capable of improvement, and against depopulation of France.

RED CROSS INFANT MORTALITY CAMPAIGN IN FRANCE *

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The work of the Children's Bureau up to January 1 was principally concerned with the immediate care of refugee and *rapatrié* children, the establishment of hospitals, clinics and refugee homes, and the aiding of both French and American child welfare societies in their work. During these first six months a preliminary study was made of general health conditions in France, as related to mothers, infants and children. These problems, outside of the immediate undertakings referred to, are not, generally speaking, acute, but simply the inevitable result of the withdrawal of physicians from general practice.

GENERAL HEALTH CONDITIONS

If one could picture cities, towns and villages practically devoid of medical and nursing service for the general population, one would have a fairly accurate idea of the health conditions in France after four years of war. The larger cities have from 50 per cent. to 25 per cent. less physicians than before. The city of St. Etienne, with a population of 180,000, had 120 physicians before the war. Now, with an increase of population, 250,000, people have the services of fourteen physicians only.

SCARCITY OF PHYSICIANS

In the villages surrounding the American Red Cross Convalescent Hospital for Children at Ste. Foy l'Argentière, our physician finds that most of them have been without a physician since the mobilization, and the establishment of clinics in these villages becomes inevitable if we are in any way to help the health situation. These two instances of a manufacturing and mining center like St. Etienne and the rural communities about our hospital show what the existent conditions are far from the war zone, and are typical of the whole of France.

DECLINING BIRTH RATE

What the accurate infant mortality rates are in France is impossible to state owing to the fact that compilation and analyses of statistics have been in abeyance. Certain general statistics are known to be fairly

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accurate. There can be no question that the birth rate in France has dropped in an appalling degree. The reason is plain. The men of France have been in the trenches for four years and the women of France have been filling their places in factories and workshops. Before the war some 5,000 women only were employed in factories. Today there are over 800,000 women so employed. The mere contemplation of these figures, the rapid exodus of women from the home, and the absence of the men in the trenches gives ample reason for the lower birth rate.

France's birth rate before the war was known to be just paralleling her death rate with a surplus margin that kept her total population a little above the level. Since the war her total death rate has increased to an extent it is impossible to estimate, but with this increased death rate and the inevitable diminution in birth rate the result today is that the birth rate is 40 per cent. below the total death rate, a figure which no country has ever reached before except as it began to pass out from among the group of first class nations. It is farthest from American thought to criticize or to cast any reflections on this situation. It is the inevitable result of a nation's heroic stand against odds which few in this country (America) have ever contemplated.

EFFORTS MADE TO REDUCE INFANT MORTALITY

It was a study of these appalling conditions which brought us to the point of attempting to do something to right them and to save the nation. The Department of Civil Affairs of the American Red Cross is attempting this in many different ways and its effect on the morale of the general population as well as the soldier in the trench is being felt in every part of France. During the past eight months I have been in almost every quarter of France and this attempt has been felt in all of them, resulting in a renewed courage as well as better conditions. The part which the Children's Bureau has undertaken in this work has already been referred to in part in the foregoing. Its direct work for the reduction of infant mortality is the means which we have chosen to affect the difference in the birth rate and the total mortality. Before the war approximately 80,000 babies died annually in France; the total infant mortality rate below one year was approximately 111. Our study showed that the government had been so occupied with the questions of war urgency that no definite program for the reduction of infant mortality had been formed. This does not mean that France was unmindful of the situation—far from it. The Senate, the Chamber of Deputies, the medical societies had all discussed the danger signals of their present situation.

WOMAN LABOR IN THE INDUSTRIES

The subject of woman labor in the factories has been the pivot of many important discussions, but the exigencies of the situation have absolutely demanded her presence. It was not a question of what was best for the future of the race, but of how to meet the acute pressure of the present. Certain definite steps have been taken to ameliorate the condition of women in the factories, most noteworthy among them being Paul Strauss' law of August, 1914, which allows an allocation of 1 franc a day for the mother one month before the birth of her child, and 1½ francs per day for four weeks after the birth of the child. This has had a powerful influence in increasing the birth rate, and it is one of the objects of our campaign to see that this law is put into force throughout the country. The conditions of the Roussel law, making it mandatory for factories to have *chambres d'allaitement* and *crêches* for nursing mothers and babies, and the creation of factory inspectresses to see that these laws are carried out, shows the earnest intent of the government to right as far as possible the deplorable conditions created by this ghastly war.

WOMEN ENGAGED IN WAR WORK

In the Academy of Medicine, throughout the whole period of the war, the discussion relating to infant mortality and the lowered birth rate has ebbed and flowed. Every one is familiar with Pinard's firm stand against the employment of women in factories. It is not for us to dispute the pros and cons of this question. The fact remains that to save France, the women had to work and the French mother preferred to work although it jeopardized the future to save the present, and who will gainsay the wisdom of her policy? We are facing facts, not theories, and in conjunction with the Ligue contre la Mortalité Infantile and the federal government, the Department of the Interior, the Service de Santè, the Children's Bureau of the American Red Cross have worked out a definite program. In the Ligue are the foremost representatives of the medical profession in France interested in women and childhood, as well as the most intelligent social workers, philanthropists and educators. Senator Paul Strauss, author of the beneficent law just referred to, is its president. Dr. Marfan, of international reputation as a pediatrician, is its first vice president. Dr. Le Sage, another well known pediatrician, is the secretary of the Ligue.

PREVENTIVE MEASURES ADOPTED

After careful study and discussion of the situation a program based on simple but fundamental principles has been adopted. The underlying principle of the program is that the simplest means are often the most efficacious; that preventive measures are far more forceful in lowering infant mortality than curative measures, and that these measures must start in the prenatal period, and must reach every mother a long enough time before the birth of her child to ensure as nearly as possible a normal pregnancy and a healthy baby. Every baby will be "followed up" so as to prevent illness.

Every one is familiar with the fact that our present preventive measures for the infant originated in France, by the establishment by Budin of the *nourrissons* clinics in 1891. These clinics exist throughout France and one of our main methods of procedure in this campaign is to see that all these clinics are functioning to their fullest capacity and that to each one is attached health visitors to follow the mother and child into the home, thereby insuring necessary medical advice at regular stated periods. Wherever such clinics do not exist or have been closed they are started or reopened. Most of the women available for health visitors and nurses have been withdrawn to the *blessé* hospitals (hospitals for wounded) and the importance and need for establishing health visitors for mothers and infants has been emphasized by the creation of short intensive courses for women who have been working in *blessé* hospitals, or who have had hospital and Red Cross training of different kinds. Such courses have been established in Paris, Lyons, Marseilles and Bordeaux, and it is to be hoped that the influence and effectiveness of these health visitors will be manifested before long in the increased attendance at prenatal and *nourrissons* clinics, and that the resulting attention and care of the pregnant mother will diminish the rising abortion figures, increase the number of births and markedly diminish the number of deaths.

These two main lines of procedure cannot be questioned. There is no possible conflict between such methods and any particular school of thought. They are obviously the common sense methods of reaching our desired results. In any given locality these methods bring us in touch with every mother and child, and strengthen existing institutions that deal with mothers and children, developing them to their fullest capacity and only creating new ones where none have previously existed, or where the needs of the locality have outgrown the existing ones.

COMPLETE COOPERATION

The unification of effort among existing and newly created institutions is one of our chief objects. This is done by bringing together all those interested in mother, infant and child, and the common purpose, that is, reduction of infant mortality, for which we are all working, has always been sufficient to establish a local program to which all contribute that which they are best equipped to give. The government, with its centralized power to put into effect existing laws, and to strengthen and enlarge their intelligent methods of public health and charity—everywhere the effective cooperation and backing of the Prefet and Mayor has been secured first and never has it been refused —and the institutions which the government has already created, have been supported.

In France, as elsewhere, private philanthropic efforts are supplementary to the governmental efforts. In some places they have attained more prominence than in others, but our aim has been to support all as impartially as possible, simply keeping in mind a unified and definite program in each locality as the great essential for the success of any public health movement.

The medical profession, all those interested in mother and child, are always brought together on a central committee, and the local problems and means for meeting them are carefully discussed, and the details for particular situations worked out. The Children's Bureau of the American Red Cross has no idea that it can in any way supply the lack of physicians throughout France. All it can aid the French Government and the Ligue in doing is to unite all available forces, governmental, philanthropical and medical, in a preventive educational program.

Wherever institutional, hospital or dispensary needs are greatest the Children's Bureau is establishing such clinics and hospitals, as, for instance, in overcrowded manufacturing centers or cities that have been forced to receive thousands of refugees from the invaded districts.

PUBLIC EDUCATIONAL WORK

To realize to the fullest extent such a program it is necessary to create and guide public opinion. For this a definite educational division of the Bureau has been established, which has already achieved much in its single traveling exhibit on infant and child welfare. This exhibit, during the months of January and February, covered the Department of the Eure-et-Loire in conjunction with an exhibit on tuberculosis prepared by the Rockefeller Commission. The results of this traveling exhibit have far exceeded our expectations. It was simplicity itself in its design and equipment, consisting of three series of panels dealing with infant and child welfare, such as the importance of breast feeding, simple hygiene, fresh air, and bathing, etc. There are five posters which call attention to the saving of the baby, and these are most popular. Three small booklets, one on the "Future Mothers," one on "The Nursing of the Child," and the third emphasizing simple hygiene, were used most successfully. A short moving picture on the advantages of nursing the baby, bathing the baby, and other methods which promote health, with a lecture illustrating the points covered by the panels and books, is much appreciated. Demonstrators, both American and French, talk of the work, give practical suggestions to the mothers, and hold short conferences with the mothers on these subjects. Some of the conferences are held in the evening for the factory women, and they are always crowded. These occasions have been brightened by serving hot chocolate on the cold winter nights to these tired women who were interested enough in their babies to come to the conferences after their hard day's work.

EXTENSIVE EXHIBIT HELD AT LYONS

During the latter part of April we carried on a more extensive and elaborate exhibit in Lyons. At this exhibit we had complete representation of all child welfare work, including prenatal, with booths, demonstrations and talks on prenatal care, the proper bath for the newborn child, a booth concerning preparation of milk and care of the baby, and a separate booth in the center of the building where the care of the baby was actually demonstrated, bathing, dressing, and proper way to have the baby sleep and play. In connection with the proper equipment for baby's room the education of young children was also demonstrated practically, as was similarly the recreational work for younger and older children. We had complete booths on dental hygiene, hygiene of the mouth and throat; work on tuberculosis was shown from an exhibit borrowed from the local tuberculosis bureau and from the Rockefeller Foundation. We had a continuous lantern slide demonstration at one end of the hall, and at the other end moving pictures of many of our best American and English films, which had been adapted to the French.

A NOVEL EXHIBIT

One of the novel features of this exhibit was the use of the French *guignol,* what we would call a Punch and Judy show. This is a national form of entertainment which in many places has the same place in entertaining the public as the moving picture has in this country. We adapted a very good scenario, demonstrating the need for breast nursing the infant, and it was so popular that we had great trouble keeping people away from overcrowding the room at all times when it was being shown. These exhibits and the educational work had been planned in the most part by Mr. Philip Platt, who has had a great deal of experience in this type of work, the success of both our traveling exhibits and our larger Lyons exhibit largely being due to his untiring work and keen appreciation of the French point of view. Lately Miss Ellen Babbitt, who was formerly with the Russell Sage Foundation, and who had a great deal to do with the Philadelphia baby show, has had charge of the arrangement and development of new material for our exhibits. We have had many voluntary aids and assistants in this work, the National Kindergarten Association taking charge of the kindergarten work, and members of the best recreational schools having supervision of the recreational field.

LARGE ATTENDANCE

The total attendance for our three weeks in Lyons was over 170,000. Between 30,000 and 50,000 school children attended it, the rest being mainly from the working and industrial class of people. The interest shown in the exhibit was perhaps best illustrated by the fact that we were able to gather all types of people together. The Mayor of Lyons, who is probably one of the most progressive and dominant characters in France, Mayor Herriot, had a great deal to do with our success. The Préfet of the Department cooperated most heartily from every point of view, the Cardinal of the diocese lent his aid, and both the general and local military authorities were at all times most cooperative and did everything to assist and to show their approval of the work. This exhibit in Lyons is the beginning of a very large center for our work, and Dr. Clifford G. Grulee of Chicago has taken charge of this department.

EXHIBIT AT MARSEILLES.

In June the exhibit was transferred to Marseilles where we developed a large exhibit along exactly the same lines and received the same type of encouragement and enthusiasm from all groups of people. Of course, the problem in Marseilles was quite different from that in Lyons, as the population is very much more diverse. Here is the meeting ground for all races and all colors. I have seen no city in all my experience that in any way is so fascinating as is Marseilles at the present time. We hope to continue these exhibits in larger or smaller dimensions in practically all the cities of France, hoping some time during the fall, if it is at all possible, to have an exhibit and conference of as many workers as possible in Paris. This in conjunction with the backing which we have at all times received from the Department of Interior, Public Health Service, of which M. Brisac is the chief, and from the National Association for the Prevention of Infant Mortality, of which M. Paul Strauss is President, both of which have in every way cooperated with us and with whom we are working out a national program. It is in conjunction with this bigger movement that the French Government and the National Association for the Prevention of Infant Mortality of France and the Red Cross decided on a visit by their representative, Dr. Paul Armand-Delille, and myself to this country, to study public health questions, especially those related to infant welfare.

SHORT NURSING COURSES

Since January, in cooperation with the Rockefeller Foundation, we have established a number of short nursing courses for health visitors, one in Paris, one in Lyons and one in Marseilles, and are cooperating with some of the French training schools for short courses in Bordeaux and in some of the other cities. These courses are to meet the need for French workers in our dispensaries, in the "follow up" work, which has been found so essential to all social medical work in our own cities. The course is mainly practical, with a minimum number of lectures, not more than one lecture a day, the practical work being in conjunction with our hospitals or dispensaries and intensive "follow up" care of the sick. In this way we are hoping to train a large number of French workers for our medical social service, not to do perhaps the actual nursing, as is done by our trained nurses in this country, but to carry on the work of following up the patients from dispensaries, both from medical and social service standpoints. It is an experiment that we feel is of great importance. Its development undoubtedly will change from time to time, but that there is need for such workers not only in France but at home, I think present conditions are proof enough to all of us. Just what this type of worker will be is, of course, very difficult to say at the present time, but some development of a new field for less highly specialized workers than our trained nurse or public health nurse is sure to result.

THE PSYCHOLOGIC TIME

What I have seen not only in France, but also in England and in this country since returning, has convinced me that now is the psychologic time to develop and coordinate all our child welfare work in this country. I feel that all the different medical associations which represent the best medical thought in child welfare should certainly get together on a definite coordinated program for this country, and back up our governmental bureaus dealing with child welfare problems. This year in America has already been proclaimed by President Wilson as the "children's year," and it will be a great lost opportunity unless some national program which coordinates all the best efforts both private and governmental is worked out and put on a very sound basis. I am hoping that every effort will be made to take advantage of this psychologic situation, and I am sure that every one interested in the problem is doing his utmost to bring this about.

THE WORK OF THE CHILDREN'S BUREAU OF THE AMERICAN RED CROSS IN LYONS*

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LYONS, FRANCE

INTRODUCTION

Up to the time when the work was started in Lyons, there had been no systematic or extended efforts to carry out civilian relief among the children in any place in France, except in the war zone. The work in Lyons was definitely not only to relieve the local situation which was greatly complicated by the appearance of many refugees and *rapatriés,* but also to attempt to educate the people of France with the purpose of reducing infant mortality. While the infant mortality in France is not high in comparison with that of some other countries, the birth rate is so low, especially since the beginning of the war, that it is necessary to reduce materially the death rate among babies and children if France is to survive as a nation.

GENERAL PLANS

Our general plans of action here consisted, therefore, in two definite efforts, one was the development of a system of dispensaries and hospitals to look after the *rapatrié* and refugee children. For this purpose it is planned to have dispensaries which will work in unison with the local charitable organizations, a hospital for infants and children, a contagious hospital, a convalescent home and a country place for summer outings.

The educational campaign, which repreesents the second effort, consists in a baby show, the training of a corps of French women as visiting nurses, the coordination of the local charitable efforts and subsidizing the same.

MEDICAL CARE

The work of our dispensaries and hospitals is not entirely devoted to *rapatrié* children, though in large measure they are taken up with their care. *Repatrié* children come in through Evian, where they remain from ten days to two weeks. When leaving there, three classes of cases come to Lyons—the orphans, the sick children and those whose parents wish to bring them to Lyons. The orphans and sick children are all assigned to the Société de Secours aux Rapatriés, which is under the direction of Mme. Gillet-Motte. The children coming from Evian are taken care of by her, unless they are acutely ill, when they are sent directly to one of our hospitals. Mme. Gillet-Motte maintains two establishments, one for boys and one for girls. In addition to these, she is now erecting barracks which will be used to take care of such patients as have been exposed to contagion in the other establishments. Such is the general plan of the medical work.

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* Submitted for publication Aug. 14, 1918.

ESTABLISHMENT OF A DISPENSARY

About the middle of March we established a dispensary at 42 Avenue Berthelet, under the direction of Dr. Virginia Murray of San Francisco. This dispensary was for the care of *rapatrié* children living in the city of Lyons, but was not limited to that work, as the medical situation here is such that the physicians welcome any aid in looking after the poor of the community. This clinic at the start was for two days a week. It was soon found useful to establish in connection with this a nose and throat dispensary which was put under the control of Dr. and Mrs. Wiggin of Boston. During the first week, the dispensary on each of its days had fifteen cases. It is being found necessary to increase the number of medical dispensary days to six, and open the nose and throat dispensary two afternoons a week. We are now planning further extension of the dispensary system. The total number of patients treated by the American dispensary during the week ending April 16 was 70.

ESTABLISHMENT OF A HOSPITAL

It was evident from the first that it would be necessary for us to open a children's hospital in Lyons, and we were able to obtain a suitable property for this purpose. This was no more nor less than a modern hospital which had been opened three months before the beginning of the war.

The physician in charge had been mobilized and the hospital closed when the war was declared. The building had not been occupied since and was in excellent condition. It represented a modern hospital in every respect, with operating suites, hot and cold water in every room, large linen closets, small service room on each floor, dumb waiter, clothes chute and even a garage in the building. The final arrangements for entry were concluded on March 30, and the first patient, a child from Evian with an acute mastoiditis, arrived on April 1. Up to the time of writing, which represents a little over three weeks, we have had fifty-six patients in the hospital, of whom eighteen remain; only one died. Our staff has been organized under Miss Butler of

Hartford, Conn. We expect a large infant ward here which will take care of between forty and fifty babies. In addition to this, the hospital will probably hold forty children, so that our capacity can probably be stretched to 100 if the situation demands it.

A CONTAGIOUS HOSPITAL NEEDED

Probably our greatest need is a contagious hospital and this we have been finding hard to procure. It seems at last certain that we have a suitable location for this work, not only architecturally but also sentimentally. We are preparing no less a place than the palatial home of the once German consul, which is located in the most fashionable part of the town and overlooks a beautiful park. This is very well fitted for the purpose, since it is divided into suites of two or three rooms, each of which has a bathroom in connection, and it would be possible to isolate several different contagious diseases in the separate suites.

About 30 miles out from Lyons there is located on the top of a hill the beautiful Chateau des Halles surrounded by an immense park which contains many different kinds of trees from all over the world. This park was donated to the Hospices Civils de Lyon by Mme. Mangini, and was taken over by the American Red Cross in November, 1917, as a convalescent home for children. It now contains about 100 children and completes the chain of hospitals which the American Red Cross plans to have in Lyons.

BARRACKS FOR REFUGEE CHILDREN

The American Red Ccross has also rented an immense property known as La Chaux, which is about 8 kilometers outside of Lyons. This property is rapidly being fitted up with barracks to hold 600 children. It is intended that it shall be used for refugee children, perhaps with their mothers, the whole to be administered by the Children's Bureau of the American Red Cross. The location is beautiful, the outlook being the banks of the Saone River over a beautiful green slope studded with fruit trees which at this season of the year are in bloom. The park immediately surrounding the building is very large and will admit of expansion of our scheme to almost any size. We also hope to be able to give some of the children of Lyons summer outings at this place.

EDUCATIONAL WORK

When we came to Lyons to open the work we had in mind certain definite schemes which must be carried through. Owing to the desire previously mentioned to reduce the infant mortality in France, it was thought wise to open an exhibition, which is known most familiarly as a baby show. For this purpose we procured the exhibit building for automobiles which is used at the Lyon's Fair. This is an immense building, 92 meters (302 feet) by 24 meters (79 feet). The immediate work of the exposition was under the direction of Mr. Phillip Platt. Mr. Platt has had a very wide and varied experience, first in New York, then in Belgium and Russia, and now in France. These had been extremely successful and it was decided to try out the plan on a larger scale in Lyons.

OPENING OF THE EXPOSITION

The exposition was opened on April 9, with a large meeting, for which invitations were issued. The mayor of Lyons, M. Herriot, presided. The principal address of the day was delivered by Professor Jean Lepine; other addresses were delivered by the Préfet, Rault and Cardinal Maurin. The meeting was further distinguished by the appearance on the platform of the Military Governor, General Ebener. Short speeches were delivered by Mr. Folks, head of the Civilian Department of the American Red Cross, Dr. Lucas, Chief of Children's Bureau, and the writer. The meeting was held in the cinema room, the seating capacity of which is about 800. There could have been no fewer than 1,200 people in the room. The following day the exposition was opened to the public. There has been an average attendance of between 7,000 and 8,000 daily. The largest single day was 11,000. The popularity of this exposition with the people of Lyons can best be gauged when we realize that the attendance for the first nine days was larger than that for the same period of the Philadelphia baby show, the most successful of such enterprises in the United States.

PLAYGROUNDS ESTABLISHED

Outside the exposition in the big Place Bellecour, there were fenced off two large plots for playgrounds, one for boys and one for girls. These were put under the supervision of expert playground workers from the United States. In the exhibit itself the special features have been the cinema theater and the *guignol*. The *guignol* corresponds in a general way to our Punch and Judy show, but by the people of France it is recognized as a moral teacher, and by this means we were able to impress on them many of the maxims which we wished to convey to them. This exposition will go on to the larger cities of France, and we trust will be perfected to such an extent that it will become more useful and more direct. It is intended to have such exhibits on a smaller scale in the different cities and towns of the region surrounding Lyons.

TRAINED NURSES NEEDED

One has to be in France only a short time to realize the dire need of this country for trained nursing. There is nothing in France which corresponds to our trained nurse. Perhaps the American Red Cross could do nothing better for France than to promote a proper respect for the nursing profession. With this in mind, there was undertaken the duplication of the efforts in Paris for the formation of a group of women whose work would correspond to that of the visiting nurses in America. To do this in such a way as to obtain the maximum result, the prime necessity was care in the selection of these women. In connection with our head nurse, Miss Sophie Nelson of Cambridge, Mass., a committee of five of the most influential women in Lyons was formed. The pupils for the course were chosen by these ladies with the idea not only of procuring women with some nursing abilities, but also of procuring those with a definite standing in the community. Of those who applied, twenty-five were chosen. Their course of work is given by the French physicians, who have cooperated most admirably in every way. This course consists of a series of forty lectures, one lecture a day being given from the middle of April until the first of June. The practical work is given by the French physician and the American nurses. Visits are made each day in groups of five to the ward with the French physician. The nursing teaching is done by the American nurses in our hospitals and dispensaries. It is hoped that these women, so trained, will be able to help us in our campaign during the summer for the reduction of infant mortality.

COORDINATION OF THE WORK

One other effort has been made by us, and that is to combine various local charities for children in such a way as to stop all duplication of effort. It means a great deal for the name of the American Red Cross that the people of Lyons have entrusted us with such an important matter. We are now establishing a section in our bureau here for the expert care of this situation. The work will be under Miss Eaton of Columbus, Ohio. Up to this time the investigation on this matter has been taken care of by Mrs. de Selincourt, an American woman, the wife of an Englishman, who is also with us and helping us a great deal. It is proposed to have the Children's Bureau in Lyons act as a clearing house for the work of the local charities. By doing this, we will be able to see where money is most needed and how it can best be expended. Up to the present time, the American Red Cross has subsidized but one local charity which deals with children, "The Consultations Budin," under the direction of Mlle. Noyer, which is receiving 2,500 francs monthly. This money is given to nursing mothers to the amount of 5 francs a week each, provided the baby shows sufficient gain in weight during that period. The idea is that the money thus expended be used in procuring sufficient nourishment for the nursing mothers. The scheme, so far, seems to have worked very well.

VACATIONS FOR CHILDREN

In addition to this, we have another definite purpose for which we will expend money. There is in Lyons a very able *maire* and municipal government. One of the chief charities which is supervised by the municipal government is one which provides for summer outings in the country for the children of Lyons. With the drain on the finances of the country which the war has produced, it is being found impossible for this to be carried out on any large scale. It is now proposed and accepted that the American Red Cross should appropriate 35,000 francs for this purpose. This insures a six weeks' vacation in the country for 500 children. The American Red Cross has taken over all of this work and every child which goes to the country will know that the American Red Cross is sending him.

CONCLUSION

No idea, however novel it may have appeared to the French people, has met with opposition. Everything which we have proposed has been patiently considered, and in most instances whole-heartedly received. The way in which they receive the American efforts to aid them in *our* struggle for democracy is in the same spirit that the American Red Cross gives its aid.

The politeness and kindness is touching. From the lowest to the highest we meet with only kind words and actions and if for no other reasons, the American Red Cross effort is worth while, because it is placing the American people in the hearts of the people of France.

A PUBLIC HEALTH PROBLEM IN FRANCE *

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FRANCE

Beginning with the winter of 1916, there arose a problem consequent to the war and the German occupation of Northern France which has had most far-reaching effects. At that time, the question of food became particularly acute in the occupied regions, and for that reason the evacuation of the unfit or useless of the civil population was decided on. By way, then, of Belgium, where there is a stop of from three days to three months, through Germany and Switzerland, with a stop of three hours at Bern, thence into France, have come constantly, with short interruptions, from 1,100 to 1,300 persons a day, of whom from 30 to 40 per cent. are children. At Evian, on the shore of Lake Geneva, is made the first stop in France. Here the *rapatriés* are first welcomed to their own country, and a redistribution made, the Préfets of the various departments having filed previously with the Minister of the Interior the number of persons whom they can accommodate. This system of repatriation has been most thoroughly organized by the French Government with the aid of private organizations, notably the Comité de Lyon.

DIFFICULTIES ENCOUNTERED

The difficulties of facilitating the passage of 1,300 persons a day through a village of 2,000 inhabitants may readily be imagined. Fortunately, large enough buildings for the vast amount of clerical detail necessary to the ticketing, billeting, overnight housing, repatriation, redistribution, military intelligence, civil intelligence and similar agencies were available. And with the arrival of this number in two convoys, one in the morning and the other in the evening, it has been possible to accomplish this extraordinarily difficult task. It is not necessary to go further into detail in regard to these aspects of the *rapatrié* situation, for they have been efficiently covered in various popular articles. To the profession, it is the medical problems offered which are of the greatest interest.

PUBLIC HEALTH PROBLEMS

These same medical problems were, extraordinarily enough, however, first recognized by a lay person, Mme. L. Gillet-Motte of Lyon.

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* Submitted for publication Aug. 13, 1918.

For some months after the opening of this war-immigration station the medical supervision was most perfunctorily and carelessly done. A sick person was seen if he made known that he was ill, but the great problem of preventive medicine—of protecting the interior of France from the dangers of such a floating population, all potential carriers of disease—was left untouched. Through the efforts of Mme. Gillet the French Government consented to send to Evian, for the installation of an efficient medical service for the *rapatriés*, a capable physician, trained in public health problems. In Major P. Armand-Delille, Medical Corps, French Army, whose work before the war in the great problems of tuberculosis, in teaching and in the laboratory, since the war at the camps of the French army at the front, in the epidemics of Salonica, was found one of the advanced thinkers of the French medical profession. With this appointment came the opportunity of the American Red Cross, and especially of the Children's Bureau. Dr. William Palmer Lucas, Chief of this bureau, had had presented to him practically as his first problem in child welfare work in France, that of the *rapatrié* children—wherever they were, but especially on their entrance into France, in other words, Evian—the "Ellis Island" for this group of immigrants.

AN EFFICIENT ORGANIZATION EVOLVED

Since the word at this station is mainly one, namely, "speed," the problem resolved itself, even more essentially than when an efficient and moderately lengthy quarantine is possible, into one of preventive rather than individual medicine. Working in close cooperation, Drs. Armand-Delille and Lucas have evolved an organization so calculated that a very efficient "net," so to speak, for infectious diseases has been drawn across this frontier. The adult problem, which has been handled entirely by the French service, has developed mostly into one of the prevention of the entrance of tuberculosis into France, either as the flagrant third stage of the disease or in its earlier manifestations. The question of the various other adult contagions such as typhus, typhoid, smallpox and similar infections, is negligible in comparison. This is due in part to the German medical supervision before departure, a more or less close observation if there is a sojourn in Belgium, a hurried supervision on the train, and a superficial examination by the Swiss physicians at Bern. Finally, in Evian there is an installation for the bathing of all *rapatrié* entries, the disinfection in the regulation French army autoclaves of all their clothes and belongings, and also an observation of the *rapatrié* himself by a medical officer.

EXAMINATIONS BY THE MEDICAL SERVICE

Following the ticketing of the *rapatriés*, by which means they are notified of their destination on leaving Evian, and of the location of their lodgings in Evian, they pass one by one the medical service. For the adults this observation includes a direct questioning of each individual *rapatrié* as to the condition of his past and present health, as to that of his family, and finally as to the condition of health in the neighborhood from which he comes. If there is anything at all suspicious, especially in relation to tuberculosis, he is drawn out of the line and sent to an examining room where specialists are assigned to make the necessary chest and other examinations. A system of hospitals has been established in Evian and nearby towns to accommodate the various categories of patients thus selected, namely, for acute conditions, for example, respiratory, kidney or other infections, for incapacitated old people, for pulmonary diagnosis and ultimate redistribution into established hospitals for the treatment of the various stages of pulmonary tuberculosis, for the two main skin diseases, scabies and impetigo, and for the contagious diseases of adults other than tuberculosis.

SCOPE OF EACH MEDICAL EXAMINATION

As can be seen, in this way the outlines of the organization are formulated. There then remain the conditions immediately related and hindering or aiding this system. They are, unfortunately, mostly the former. In the first place, a very quick passage through Evian is necessary. The village is too small to allow of an efficient quarantine, and an inefficient quarantine, one not allowing of effective isolation and observation, would be naturally worse than useless. The agglomeration of people is always dangerous. If they are originally subject to suspicion from a contagious standpoint and are also in a more or less poorly resistant state of health, conditions could easily become deplorable.

THE HOUSING PROBLEM

A second factor, then, with a most direct relation to the prevention of the propagation of disease, is the housing problem. It is necessary to have in Evian constantly accommodation for from 3,000 to 5,000 persons. This is made up of three categories: (1) persons awaiting members of their families in hospitals; (2) persons obliged to await news from relatives who reclaim them in one part or another of France, and, (3) finally the regular daily convoy, with its quota which must be housed for at least twenty-four hours. Naturally the difficulties are enormous, involving the question of actual hygienic lodgings, of bed linen, of adequate disinfection and cleansing of clothing and linen, of the many, many details incident to a floating population of that size. One can never attain perfection, but certainly the medical service of the *rapatriés* has accomplished a most admirable result with the help of the American Red Sross in the supply of necessary materials for the perfection or partial perfection of an ideal.

CHILD REPATRIATION

It is now possible, after showing briefly the general plan of the *rapatrié* service, to take up the particular problem as shared by the American Red Cross. This is the one of the child *rapatrié*. Dr. Lucas in his capacity as government-appointed Medical Chief of the service for *rapatrié* children has installed at Evian, in collaboration with Dr. Armand-Delille, an organization designed to handle effectively this opportunity. As I have said, our problem is, as with the adults, one of contagions, but in its way much more diverse than that of the adults. In other words, the number of contagions to which the age of childhood is subject is very much greater. We are obliged to prevent the entrance of varicella, diphtheria, scarlet fever, measles, pertussis, epidemic parotitis—in a word, the whole list of the exanthems. To see twice a day, within two and one-half hours, the time allowed, from 200 to 400 children; to rapidly examine the exposed skin surface, the teeth, mouth, pharynx, palpate the glands, and to form an opinion of the condition of that child from a public health standpoint is indeed a work which taxes one's ability to the utmost, especially if he is one who recognizes the responsibility resting on his shoulders. He is the sieve; it behooves him to have the meshes very fine. A suspicious or flagrant case of contagious disease discovered in this examination is then sent to the American Hospital.

THE AMERICAN HOSPITAL

This hospital, established in a former summer hotel, accommodates 180 patients. We were fortunate in finding a location well supplied with water, with bathrooms, service rooms, excellent kitchens, and with a separation of rooms and corridors capable of allowing of the grouping of patients into isolated wards. A cubicle system, by means of washable curtains, has been installed, to facilitate, as much as possible, the work of the nurses in effectively isolating each patient even in the same ward. Naturally, next to the task of discovering and sending to the hospital patients who have contagious diseases, probably the most important one is to prevent cross-infections. This is hard enough at best with the most perfect equipment and highly trained help. In a war-time hospital, one improvised within three weeks, to handle such a problem of contagious disease, one naturally employing other than graduate nurses, we feel justly proud of a percentage of cross-infections of less than 2 per cent. of over 1,300 entries since Nov. 5, 1917. The grouping of the first half of this series of cases is shown in Chart 1.

CLASSIFICATION OF THE PATIENTS

Naturally the children's service at Evian can only hold cases actually infected or suspicious of infection in the hospital. Among the most important reasons for this is the need of evacuating almost as rapidly as entrance is made into Evian. Our first inspection is all that is possible, except in two other categories of cases: (1) those patients capable of absolute control, and (2) patients with whom only partial control can be carried out.

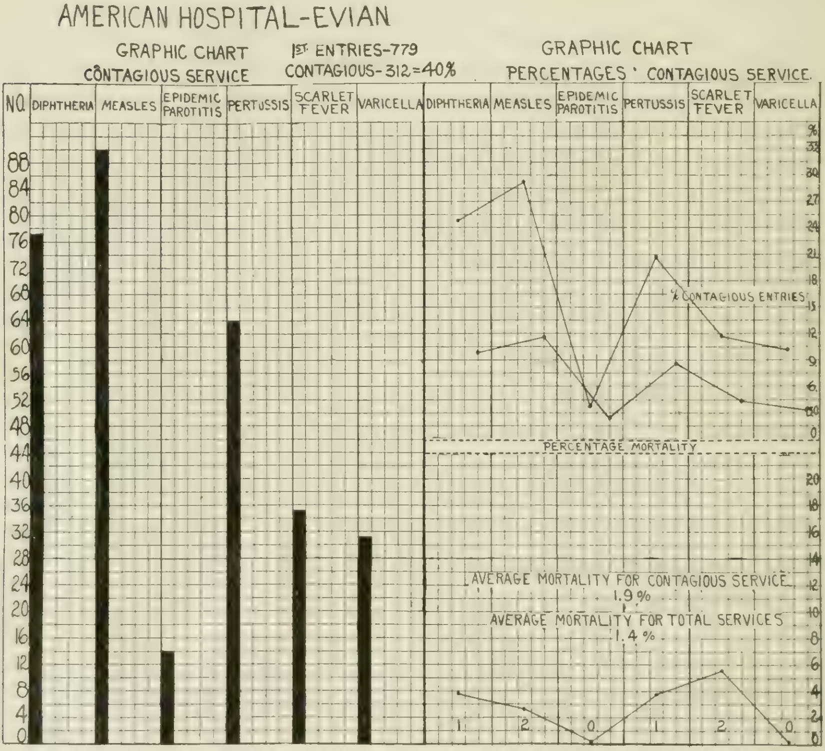

Chart 1.—Graphic summary of the cases received in the contagious service at the American Hospital. The average mortality for the contagious service was less than 2 per cent.

The *first group* constitutes the class of orphaned or abandoned children passing Evian with the convoys. These are all ultimately destined for the orphanages of the city of Lyons. On the estate occupied by the hospital a villa accommodating forty beds was available. With this at our disposal and the setting aside of a portion of the hospital to serve as an admitting ward, a period of from eight to ten days was considered sufficient to eliminate a large proportion of contagious diseases from admittance to Lyons. With the same cubicle system as employed in the remainder of the hospital all orphans are admitted to this ward, isolated for three days, during which cultures for the presence of carriers of diphtheria are made, a prophylactic of diphtheria antitoxin administered, and a vaccination against smallpox made. They then pass to the villa for an isolation, at least as regards any other children, for the remainder of the period. Then in sanitary cars they are sent to Lyons. Since the installation of this service 250 orphans have been thus cared for without a single case of infectious disease being transmitted to Lyons. It can easily be seen that under such ideal conditions, comparatively speaking, all diseases of this nature might be prevented, but naturally it is only a small group capable of such treatment. For the great mass it is not feasible.

The *second group*, which may be partially protected, rests in those children awaiting their parents ill in hospitals in Evian. They are consigned to villas rented for the purpose under the care of the Comité de Lyons. Our relationship with them consists in a medical supervision and the administration to every entry of a prophylactic against diphtheria. Further than that we cannot go. A quarantine is not permitted. They are allowed to visit their parents in hospitals, to roam the streets, to visit the convoys as they arrive in search of friends, in other words, so to place themselves subject to contagion that no responsibility could be accepted by the American service. Nevertheless, we accomplish something, and as every one who works in France must sooner or later know, he is not at home, it is not his country, their laws are not our laws, their psychology not our psychology. Compromise, not unalterable methods, is needed to serve.

THE PSYCHOLOGIC SIDE OF THE WORK

In regard to psychology, it is here perhaps appropriate to speak of this aspect of the *rapatrié* situation in its relation to medicine. It is a distinctly peculiar and isolated one—one not to be encountered any other place in France or in the world. Arriving in Evian after three years without news, separated from family and friends, forced to leave their homes and belongings, they are immediately confronted, for example, with the statement that their child has a contagious disease and must be segregated ; then the reaction is intense. It is intense with a French woman in ordinary situations. Make her a *rapatrié* French woman and a new and powerful influence is presented. To the tact and discretion of the workers on the American service has been due the possibility of our accomplishing our work, but it has meant compromise. For instance, in spite of our hospital being essentially a contagious one, with all the difficulties which that entails, one must allow visiting hours—and frequently. It is a responsibility we do not care to take, but is obligatory, by reason of this same peculiar psychology. However, by means of careful observation on the part of the nurses, the wearing of long gowns and of caps for the hair, the washing of the hands before and after visiting a child, it has been possible. An appreciation of this distinctive psychology of the *rapatrié* is necessary for the work among them. Clash with medicine and especially preventive medicine it certainly does; nevertheless it is an influence so strong that it cannot be disregarded.

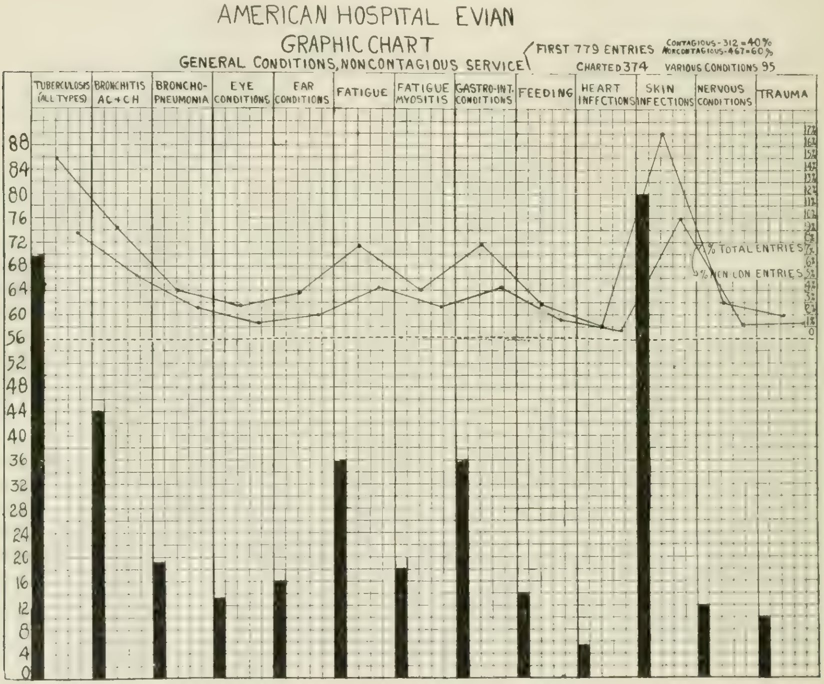

Chart 2.—Graphic record of the conditions observed in the noncontagious service at the American Hospital. The wide range of conditions which this chart covers should be especially noted.

JUDGMENT NECESSARY IN SELECTING PATIENTS FOR TREATMENT

Naturally, as one watches his file of children pass day by day, many cases, noncontagious certainly, but much in need of hospital treatment, are found. Judgment is necessary in choosing them, for the holding of one child usually means a family of six or eight who must be lodged for the period of hospitalization. Nevertheless, we have been able to care for a considerable number of cases of noncontagious disease covering a fairly wide range of conditions (Chart 2).

For the ambulatory patients a general dispensary, which has seen an average of twenty-five children a day, is established near the hospital. Here are brought by means of ambulances with a nurse the many slight infections and traumas incident to the voyage, and also those cases suspiciously suggesting a general condition of one sort or another, particularly tuberculosis.

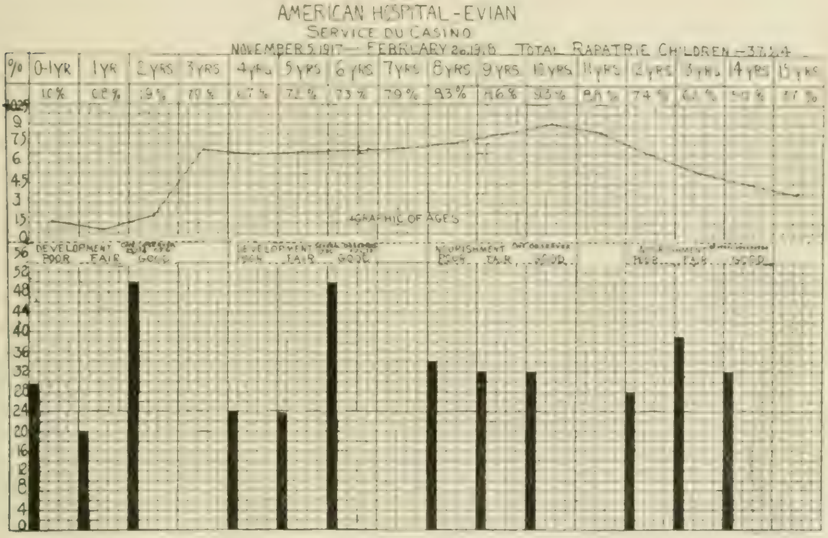

Chart 3.—General survey of the ages, nutrition and development of the children treated at the American Hospital from Nov. 5, 1917, to Feb. 26, 1918.

SUPERVISION OF THE FAMILIES

In conjunction with the adult service, for every case of tuberculosis in a child, no matter what type, requiring hospitalization, first at the American Hospital in Evian, later the convalescent hospital of the Children's Bureau at Lyons, and ultimately for a tuberculosis hospital such as is maintained by the same bureau at Cavalaire on the shore of the Mediterranean, an *affiche* is made out which will be sent to the Préfet of the department to which the particular family is directed. He, in his turn, will thus have data relative to his new population, and also will be able to furnish details to the local physicians. This method is employed not only for our patients coming for examination to the dispensary and showing evidence of active tuberculosis, but also for those hospitalized for a short period at Evian and refusing a longer hospitalization. As an active adjunct of the general dispensary, a dental dispensary is maintained which forms a most satisfactory part of our work in attempting to relieve actual individual necessities. To this dental dispensary are sent the children of families who are to remain in Evian for some days; that is, the orphan class previously mentioned, before they are sent to Lyons, and the noncontagious patients in the hospital before they are discharged. This we feel to be one of the most constructive of the divisions of our work. We are exceedingly fortunate in having in the person of Dr. Raymond Watson of Waltham, Mass., a man most peculiarly fitted for this situation.

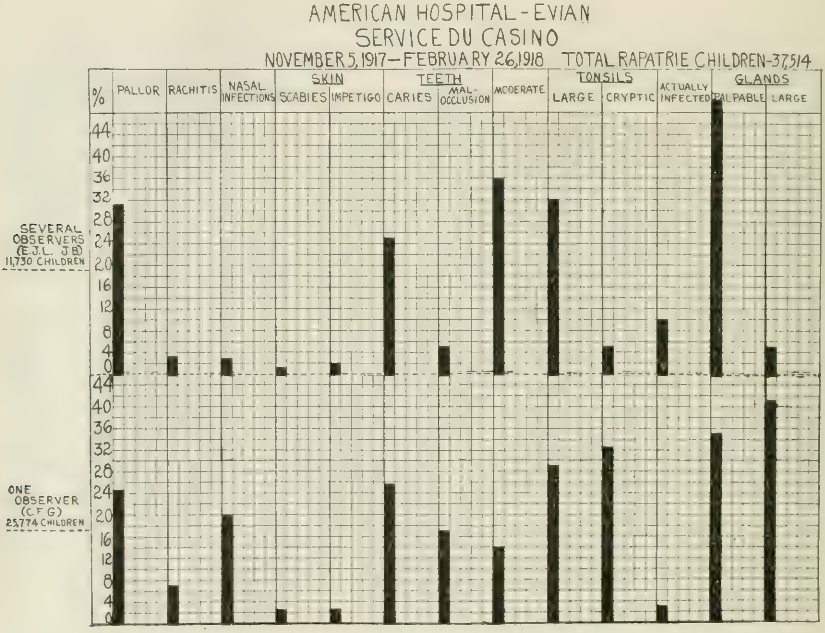

Chart 4.—Graphic summary of the conditions and diseases observed in children at the American Hospital. The number of repatriated children examined totaled 37,514.

MEDICAL CONDITIONS ENCOUNTERED

Insofar as the medical data which are encountered in this service are concerned Charts 3 and 4 explain conditions as we find them better than words. The examinations of the children as they pass are necessarily superficial, but serve, from the public health standpoint, equally well as a more complete one. And it is the public health, the preventive medicine situation, which is our main problem. From the side of individual medicine, of course, much more could be done, but that must be left to the departmental workers among the *rapatriés* when they reach their ultimate destinations. What is accomplished at

Evian for the child himself individually is done over and above the primary problems and always against many difficulties. It is an axiom in this service that "a person able to travel must move on with the convoy." He must wait for his cure. It is only those too ill to travel or dangerous to others who may be allowed to occupy space in Evian. Thus is our problem limited. Perfection in the organization, however, is progressing, and with that improvement come increased possibilities for other lines of endeavor. Certainly the Red Cross is doing a valuable service and in such a way that friendly relations are promoted, an actual need filled, a missing cog replaced without friction in an existing French organization. This is one of the main aims of the American Red Cross — we hope at Evian to have that an accomplished fact.

In conclusion, may I state the definite thanks due to the various members of the American staff who have made our success a real one? Without Mr. William C. Stevenson of Pittsburgh, who has accomplished the actual installation of the hospital, whose active cooperation has always been so ready and willing in this difficult situation, failure would certainly have resulted. Also to the medical staff, some who have only remained a short time, but with definite service — Capt. Marshall Pease, M. R. C., U. S. Army, of New York, Dr. Edmund Labbé of Portland—but especially the Drs. Florence and Dorothy Child of Philadelphia, whose adherence to a necessary duty has been an example of willingness to serve rather than to gain well worth emulating. The daily sacrifice of the nursing profession is much the same in peace or in war. Certainly an exhibition of this service has been seen these past months in one of its most admirable forms. Actively cooperating with the medical staff in an appreciation of the problem and its responsibilities, the nursing personnel under Miss Helen Bigelow of Boston has made our work possible.

THE AMERICAN RED CROSS IN THE MEURTHE-ET-MOSELLE *

MAYNARD LADD, M.D. (Boston)
Major and Assistant Chief, Children's Bureau, American Red Cross
PARIS, FRANCE

The story of Toul is the story of the development of the civilian work of the American Red Cross in the department of the Meurthe-et-Moselle. The little walled city surrounded by some of the most formidable fortifications in France has never in times of peace been a place of great importance. In times of war, however, Toul has always figured largely in the events of the day, and has proved the backbone of the defense of old Lorraine. Now, in the fourth year of the war, when America enters the world's struggle and seeks through the activities of the American Red Cross to show to the French people the depths of their admiration and sympathy, we find that Toul has become the center about which all the civilian relief work naturally groups itself.

ENVIRONMENTS NEAR TOUL

From the top of the hill of Dommartin on which our barrack hospital rests, one sees a wonderful expanse of country. The city of Toul rests in the valley at our feet, deep-moated, high walled, its great cathedral rising like a mighty sentinel in the midst of quaint and ancient gray stone houses. Fort St. Michel, a miniature Gibraltar, towers higher than our hills, higher than the great cathedral, its guns pointing up the valley where, some kilometers away, rest the khaki lines of America's first army in France. A little to the right one sees the hangars of a former French aerodrome, now occupied by the first squadron of American aviators. Some of us were fortunate enough to witness the first clash of hostile planes with our own, when Campbell of Harvard and Winslow of Yale turned the tables on an over-confident and arrogant enemy. Still further to the right are the great automobile repair shops of Jean d'Arc, and one knows that over there beyond the hills are other aviation camps, military hospitals and munition factories. In other words, we are the center, geographically, of a place teeming with military and industrial activity, but from all of these we are so removed from Hun objectives that it is unlikely that their bombs will drop on our twenty or more red-crossed roofs by accident. If the Boche comes by design for purpose of reprisal, it matters little to them whether we are on the top of our little hill, or 10 or 15 miles

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further from the front. From shell fire we are protected by an obstinate and efficient line of boys from home, flanked by the sympathetic and indomitable *poilu*. Here at Toul we find the strategic center from which our work naturally radiates out into every corner of Lorraine; from Pont-à-Mousson, where our dispensary is within fifteen minutes' walk of the trenches, down along the battle line to Emeville, where American blood was first shed in France, and further still to Epinal in the Vosges.

OBJECTS OF OUR WORK

There are two ideas underlying our work at Toul. There is the medical and civilian work for the relief of suffering among women and little children deprived by war of their own doctors and hospitals. Then there is the effect of this work on the morale of the people, and so indirectly on the army. A *poilu* was fighting in the trenches when his wife's letter told him of the illness of his child. He secured "permission" and hurried home, but long before he got there we had the child comfortably stowed away in a hospital cot at Toul, and when he finally came to us the child was well. The grateful *poilu* thanked us with tears in his eyes and said that now that he was not worried about his family he could go back to the trenches with a light heart and ready for any chance. This is typical of many cases, and with the extension of the work, following a broad, comprehensive plan of operations, the American Red Cross is going a long way to do for the community what it did for the individual *poilu;* it is relieving the people of worry which comes from trying to carry too heavy a burden. It does not take a psychologist to gage the effect of such relief, if effectively and extensively applied, on a population that is trying to maintain the industrial activities of their region in the face of nightly raids from avians and the more insidious, but equally potent propaganda which filters through from Hun lands.

EARLY HISTORY OF OUR ORGANIZATION

The early history of Toul has been told many times: Briefly, the work started by the joint efforts of the American Red Cross and the American Fund for French Wounded, had its origin in an effort to give homes to the children in the munition towns about Nancy whose houses had been destroyed by bombs, and yet whose parents must remain to work in the *usines*.

Cooperating with M. le Préfet Mirman, and the French civil and military authorities, the newly erected military barracks at Luxembourg Dommartin, Toul, became the seat of the present Asile Caserne du Luxembourg. The development and management of this institution was one of the very first undertakings of the newly formed Children's

Bureau of the American Red Cross under Dr. William Palmer Lucas, chief. On Aug. 17, 1917, Dr. J. P. Sedgwick took over permanently the temporary organization which had been effected by Mrs. Lathrop of the American Fund for French Wounded and Mr. Robert Davis and staff, and which had been directed by Mr. MacCormick. He was assisted by Dr. N. O. Pearce of Minneapolis, and Dr. Douglass Durand of Seattle. On Dec. 1, 1917, Dr. Sedgwick and his staff was succeeded by the writer assisted by Drs. Karlton G. Percy and Robert G. Sharp of Boston. To the new management was given the directorship of the medical civilian relief in the whole department of the Meurthe-et-Moselle.

ESTABLISHMENT OF REFUGEE HOMES

The Asile Caserne du Luxembourg has, at present, accommodations for 550 refugees. These are for the most part young children. There are about thirty-five mothers. A school for the older children and an École Maternelle for the little ones is provided by the French government. The care of the children is under the direction of Miss Stotend, assisted by French aides. Classes in sewing and manual training have been established and gardens laid out for each *battement,* to be worked by the children, in healthy and instructive competition with each other. In the reorganization of the refugee department, we have had the invaluable assistance of Mr. R. R. Reeder, chief of the New York Orphanage. The children are well fed and well clothed, and the general health of the group may be understood when one states that over 500 children have been cared for over a period of nine months with no illness so serious as to result in death.

ESTABLISHMENT OF THE HOSPITAL

The hospital at Toul had its origin in the necessity of providing an infirmary for the refugee children who became ill, and for the very small run-abouts who needed more individual care than could be given them in the *battements*. Under the new management, this infirmary has been increased to a medical and surgical hospital for children and women of 200 beds, of which forty are reserved for maternity cases. This hospital has become the medical center for the whole department, a place to which the sick poor may be taken, as they are searched for and found by our system of dispensaries and social workers. It is at present under the immediate control of Dr. Sharp, assisted by Dr. Lowe, to whose efficient work all credit is due. The 160 beds are in full operation. Forty ether operations a week represent its present surgical activity. There are thirty-six patients in the maternity wards. We operate an ambulance service, collecting patients from many different parts of the district, and not a day passes that we do not have the pleasant experience of receiving patients many of whom have walked or been carried many kilometers that they may be cared for by the American physicians.

HEALTH CENTERS

By an harmonious and effective working agreement with the American Fund for French Wounded, the American Red Cross has developed an extensive system of dispensaries and health centers. Along the course of the Meurthe and the Moselle rivers are many large manufacturing towns, devoted at present to the production of munitions of war. These towns, incapable of expanding readily to meet the increased demand on them, are crowded in many places to double their normal capacity, largely by women workers who of necessity bring with them their children, whose fathers are in the trenches. It is in such small cities, and not in the healthy rural towns, that the need arises for increased medical care and supervision, more especially as the inadequate civil hospitals have for the most part been closed or commandeered by the *militaire*, and the civilian doctors reduced to a totally inadequate minimum. It is in just such places that we are establishing the joint dispensaries of the American Red Cross and American Fund for French Wounded.

PLAN UNDER WHICH THE WORK IS CONDUCTED

The scheme under which the present management, ably assisted by Dr. Percy, is working, is as follows:

Base dispensaries are established in some central town of industrial importance, from which the needs of surrounding towns may be met by organized clinics and district visits. A dispensary "Unit" consists of a physician, an experienced head nurse with one or two aids, an automobile and a driver. The "unit" lives at the base. Suitable quarters for the clinics are obtained from the civil authorities, generally free of rents. A base of supplies is organized, and clinics are held generally two or three times a week in the larger towns, rarely once a week in the smaller places. Each base dispensary will average about five subdispensaries, but the number of towns reached by this system is, of course, much larger, as people come to us from hamlets and villages from a large radius. The clinics generally average between thirty and thirty-five, but sometimes run as high as eighty. In character they are essentially the same as those we see at home, with a much larger percentage of skin and vermin diseases.

These dispensaries serve the means by which we get a line on the really sick and surgically needy children in the community. They are the sources from which we recruit our patients for the hospital at

Toul. They also serve as a center for the distribution of civilian relief in the way of clothes and food. In the latter respect great care is taken not to distribute charity in a wholesale or socially demoralizing manner. Our procedure is to make an applicant fill out a blank stating the number of adults and children in the family and the total wages or allocations of each one. This is then submitted to the *sous-préfet* or *maire* or a committee appointed by one or the other, and the claims investigated and approved. If just, relief is afforded according to a regular scale depending on the number of children and the total income of the family.

We also secure through the dispensaries names of many expectant mothers. To each of these we give a *layette* and enroll her for prenatal care and later for a healthy babies' clinic. Often we will take a mother and all her children to Toul, placing the children in the refugee home and the mother in the hospital, for a period of a week or ten days previous to labor and for two weeks thereafter. When a mother leaves the hospital her baby's case record is sent to the doctor of the nearest dispensary and the mother is told to report there regularly. We are trying so far as we can, with limited resources and under great difficulties of conveyance, to follow up those who neglect to keep in touch with the clinic.

Base dispensaries such as I have described are now in operation at Toul, Foug, Nancy, Neuf-Maison, Lunéville, Gerbervillier and Epinal. The number of subdispensaries is constantly increasing, and the area reached is ever widening.

ASSISTANCE AFFORDED BY INDUSTRIAL CORPORATIONS

We are making a great effort to secure the interest and even financial assistance of the directors of the *usines* in all this work. Often the rooms for the clinics are furnished to us by them and in certain places they have cooperated to the extent of making financial grants. At Epinal, for instance, each of the two *usines* has contributed 3,000 francs for a *crêche* for nursing mothers, to be situated near the factories, and have agreed to arrange the hours so that the mothers may leave their work at intervals to nurse their babies. At Foug, M. Cavalier, director of the *Fonderie de Foug*, has given us the land, labor and material for a new hospital and dispensary; the American Red Cross furnishes the heating plant and equipment. So by securing their interest and cooperation now, by acting always in consultation with the *préfets, sous-préfets* and *maires* we have in mind not only the immediate practical effect of their assistance, but the prospective weight of their influence to continue after the war these practical measures of health and social relief work.

MATERNITY SERVICE

In the maternity hospital of forty beds, founded as an emergency measure in twenty-four hours, owing to a bombardment of the Maternité at Nancy, we are trying to establish a maternity service on a higher basis than usually obtains when a system of midwifery predominates. We are making the service as perfect as circumstances permit, trusting that the example may, as leaven, exert its influence much further than would be indicated by the size of the hospital. We have found the French mothers very receptive to American methods, and even the pupil midwives, whom as an experiment we incorporated into our nursing staff, have shown the greatest enthusiasm for their work under the new conditions. More than half of our nursing "aides" are young French women to whom we are giving training in American methods. These will form a nucleus around which to build a nursing force for the continuation of the better part of our work when in course of time it is necessary to withdraw the American nurses' aides.

ATTENDANCE CONSTANTLY INCREASING

The attendance at our hospital and dispensaries and clinics is constantly increasing. The need for physicians and nurses grows with each new project successfully launched. Already we have reached a record of 2,000 consultations a week. There is a field for further extensions of this kind of work, in which we have so far had the unqualified support and sympathy of the French medical, civil and military authorities.

AMERICA'S DEBT TO FRANCE*

J. H. MASON KNOX, Jr., M.D. (Baltimore)
PARIS, FRANCE

We hear much today of the debt which France, whose soil is drenched with the blood of her brave sons, and whose material resources have been drained during these years of devastating warfare, owes to the unselfish and gallant aid which American soldiers and civilians are so generously furnishing.

It is indeed an indebtedness gladly acknowledged by the French people of all classes, from the high officials to the lowly *poilu*. With our own shores protected by distance from the successful invasion of the enemy, when it became apparent to our people that the issues at stake were those of democracy versus tyranny, or the right of a free government as opposed to the might of an oppressor, our whole nation, with wonderful unanimity, entered into the conflict and is crossing the seas today to put all our resources at the disposal of those countries which heretofore have borne the brunt of the trial and suffering. "What is ours is yours" will be quoted with approval when the war clouds have long since passed away. We are indeed helping France today and glory in it, and will continue to pour into her lap our best treasures until the need is past.

RESPONSIBILITIES OF AMERICA

It is, however, to the other side of the shield that I should like to draw attention, and see if the opportunity which, as a nation, we have grasped so readily to come to France, to accept her hospitality and her good will, may not, both directly and indirectly, be of incalculable advantage to our own people, and if we take part by unselfish and intelligent effort in helping solve the numerous vital problems which press for solution in France at this time, will it not strengthen our hands at home? Will not the endeavor to understand, to assist in meeting the acute needs of the French people, make a stronger, more thoughtful, more efficient race in America? Must not the kindly, almost pathetic confidence with which Americans everywhere in France are today received, carry with it for us great responsibilities which, if bravely borne, will result in higher average capacity for service at home than ever before? Ought we not to realize the great value of the unique opportunity America has to see, at first hand, this fascinating French civilization and to work hand in hand with the many organized *oeuvres* which are devoting themselves to solving their problems?

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Truly, there is much here to see for those who have the vision. There is much experience to be acquired for those who are able to learn and those who have seen the vision and profited by their experience here should be able to see and know the way of efficient service and walk more sturdily in it at home.

PERSONAL OBSERVATIONS

I want to limit my remarks to conditions which have come under my personal observation — those having to do with many phases of infant welfare work that have been developed here in the work of the Department of Civil Affairs, American Red Cross, and particularly of the Children's Bureau. At the outset it must be understood that those of us who are working in this interesting field have great and unaccustomed resources behind us, due to the generosity of the American public. Most of us, physicians, social workers and nurses, have a prestige, as representatives from the great allied republic, which we do not have at home. Both of these unusual circumstances ought to make it possible to accomplish results here which we have perhaps long dreamed of, but have been unable to attain at home.

Let us go over a few of the classic divisions of infant welfare work and see how they are illustrated in various ways by French organizations from which we, as Americans, can learn. And at the same time let us understand in what direction our own efficiency as workers in the field of child welfare could be increased because of the unusual opportunity here.

CARE OF THE EXPECTANT MOTHER

There are, in France, a large number of excellent organizations, offering to women before their children are born, competent obstetric care and instruction and oversight during the first two years of the infant's life. One of the most important of these is "la Mutualité Maternelle," where, for the payment of 3 francs a year, all these benefits can be obtained. This organization has more than fifty consultations in and about Paris and many others throughout France. Each member of the organization receives 12 francs a week for four weeks after the baby is born, on condition that she abstain from work, and 10 additional francs if she is able to nurse her child. The results obtained are excellent. We have been able to cooperate with many of these *consultations de nourrissons* and in several instances the Children's Bureau has conducted them itself, because the French physicians have been called to military service. It would be possible to return to America, therefore, with first hand knowledge, after a considerable experience with this established and widespread effort to care for the expectant mother, to prevent her overwork, to secure good obstetrics and to encourage the breast feeding of her child.

We are cooperating in a similar manner with other organizations conducting *gouttes de lait* and other consultations, notably those started by Dr. Budin and now conducted by Mme. Budin, herself a trained nurse, in memory of her husband. It may be recalled that all our milk stations at home were patterned more or less after the Budin clinics begun in 1891 and 1892.

NURSES' TRAINING

Perhaps one of the subjects for lively discussion at home is the question of the comparative value of nurses of specialized versus general training in public health work. There is opportunity in Paris to see at close range the results obtained by both groups of nurses. Several of our dispensaries for children and infants are conducted by specialized pediatric nurses, whereas others are health centers in the larger sense of the term, where all ages are treated and the nurses have a general professional and social training. A few months' experience of this kind will help greatly in determining by which group the needs of the infant population can best be reached.

Again, the most effective method of cooperation between dispensaries having to do with the tuberculous and those treating children can be studied well at first hand in Paris. Together with the Rockefeller Foundation for the Study and Relief of Tuberculosis, in one *arrondissement* four dispensaries for both children and patients with active or latent tuberculosis or who have been exposed to it, are under way. It is the object here, not only to remove advanced cases into institutions, but to furnish adequate instruction and nursing supervision in the home, so that the spread of the disease there may be eliminated. With those having this important work in charge, our infant welfare nurses are working hand in hand, and we hope many practical lessons can be learned as the result. All children who have come in contact with known cases of tuberculosis are kept under frequent observation. Sanitariums and homes in colonies are provided for them where necessary.

SOCIAL SERVICE

In connection with all our dispensaries, social service is emphasized. This, perhaps, is America's principal contribution to the French hospital and outpatient work, although there are several societies here of recognized merit, which have done excellent work for years in this field.

Our aim here has been to assert that intelligent dispensary diagnosis and treatment cannot be successfully carried out without a knowledge on the part of doctor or nurse, or both, of the home conditions under which the patient lives. Very often, when these are found to be directly harmful to health, their correction proves to be all that the patient needs. This is the attitude of a small but growing number of our hospital superintendents and physicians at home, and here in France we have an unusual opportunity to test its value.

We have been particularly fortunate in having for several months Dr. Richard H. Cabot in charge of a large central dispensary, in Paris, where French nurses and aids have received special instruction as to the best methods of social service as applied to dispensary work. The importance of visiting in the home, on the part of nurse or doctor, cannot be overemphasized. We have been able to demonstrate, many times, the great improvement in the health of the dispensary patients who follow suggestions made at their homes by the visitor, as to food, fresh air, and general hygiene, and our Bureau has been able, on the basis of first hand knowledge, and in cases of definite need, to improve housing conditions, to increase the food supply or to increase the ventilation, with very happy results. For the general direction of our Paris dispensary work, our Bureau has been most fortunate in securing the skilled and devoted services of Dr. John B. Manning of Seattle.

WORK IN THE RURAL DISTRICTS

Thus far, in America, the principal effort to reach the baby has been confined to the cities. We have long known that the child in the country needed help. Here in France, particularly in the rural and semi-rural districts, near the war zone, where a considerable civilian population has remained, an exceedingly important work has been organized, to aid the children. Usually our dispensary equipment has been installed in some center, and from this point, by means of an automobile, carrying doctor and nurse and nurse's aide, the surrounding towns and villages are visited once or twice a week and large clinics held. Sometimes a nurse and an assistant live in one of these centers and spend the time between the doctor's visits in home visiting and in collecting cases for the clinic. Often these dispensaries have been conducted in connection with a central hospital which receives those children which require hospital care. Frequently the arrival of the American doctor and equipment has brought the first medical attention in months to some of these villages. I believe that much the same thing can be done in many of the rural districts at home, where now there is much need. Many cases requiring surgical and other special treatment could be found and helped. I have personally seen, a number of times, the joy with which the arrival of the doctor is welcomed in these small dispensaries. This rural work was begun by Dr. J. P. Sedgwick and continued and much extended by Dr. Maynard Ladd of Boston.

VALUE OF CHANGE OF CLIMATE

We have had, too, in France, a splendid opportunity to observe the value of change of climate in conserving the health of children. For years, the school children of Paris have been moved for part of the summer in so-called vacation colonies to the country—sometimes in groups of children, sometimes with their parents, sometimes to the seashore, sometimes to the mountains—or again sometimes simply to the nearby less crowded communities. All these groups form a basis for interesting study. There is much material at hand as to which kind of climate will most benefit certain conditions.

THE DEPENDENT CHILD

Again, the question of the dependent child can be nowhere better studied than here in France where orphan asylums of all varieties, in the cities, in the country, with industrial training, and without it, abound. Moreover, there are a number of organizations engaged in the intelligent placing of children in colonies in foster homes and elsewhere. Perhaps we, in America, in our politically controlled institutions, have sinned against the dependent child more than in Europe. These unfortunate children are frequently crowded into unhealthy asylums, inadequately fed and taught, and deprived of any semblance to normal family life. In many of our states, there is no proper supervision of the institutions receiving state appropriation for the care of state wards. On the other hand, the satisfactory results that have been obtained with orphaned children when they are properly cared for and educated, particularly in foster homes, is well known.

The Children's Bureau in France has received appeals for aid from scores of orphanages and asylums. In many instances, the help granted has been conditioned on the installation of improved methods, such as industrial training, with adequate supervision. At times, it has insisted on a system of child placing as a substitute for asylum life. The large number of children orphaned by the war gives the greatest incentive to an agency such as the American Red Cross pledged to the real relief of the civil population of France, to do what it can to assist these unfortunate boys and girls to secure that mode of life and living conditions which will most likely draw out their best qualities, and make of them sturdy, self-supporting citizens.

On a small scale, the American Red Cross has made itself directly responsible for the training and education of a number of war orphans adopted by our American soldiers. These children are placed in carefully supervised homes and given that education best fitted for their capacities. We hope this effort will serve as an example of what should be done on a large scale, not only in France, but in America, for children bereft of parents, and we expect that the future of these American wards will be so satisfactory as to make it necessary to give all dependent children an equal chance.

THE ILLEGITIMATE CHILD

The problem of the unmarried mother and her babe is even more acute in France today than at home. It is being met adequately here, as with us, in only a small number of instances. They are sufficient, however, to prove abundantly the contention that the life of the baby and the future of the mother depend on their remaining together throughout the first year. We are attempting to bring this about by way of example, in certain districts. We hope that in this field the willingness of the French people to follow the suggestion of Americans at this time will lead to a permanent betterment of the condition of this unfortunate group. We recognize here a special responsibility born of power to help, which we must not shirk.

INTENSIVE INFANT WELFARE WORK

One of the most valuable contributions to child welfare work which this American invasion of socially trained doctors and nurses at this critical time in France can make, both in city and rural districts, is the demonstration of methods by which necessary aid can be provided for *every baby* born. This is an ideal toward which many of us have looked impatiently at home. In no community in America has this desired state of affairs been attained. Here in France, with accurate statistics of births and deaths which have been placed at our disposal by the government authorities, there is a golden chance to demonstrate what this kind of thoroughgoing infant welfare work will do in the actual number of lives saved. We have, in several instances, secured lists with the names and addresses of all children born in the quarter of the *arrondissement* in which our dispensaries are situated. We propose, with French nurses and social workers, to visit every baby there, to follow them to the country, if they have left Paris; at any rate, to see to it that they receive adequate care. The same aid will be given in certain rural districts and in certain of the middle-sized towns. We firmly believe that the opportunity is unique to write Q. E. D. concerning the efficiency of a number of methods the efficiency of which, up to the present time, has not been actually proved. We are convinced that one of the most important legacies which we can leave in France, after our return home, is the actual demonstration from the statistical standpoint, of the efficiency of our infant welfare work in certain specified areas. If, through carefully arranged clinics, in connection with thorough social visiting, we can demonstrate a fall in the death rate among infants of 50 per cent., our work must be continued when we leave. In France, as perhaps nowhere else, the value of child life is appreciated, and almost any sacrifice of time and money will be made if practical methods of conserving the children of the nation can be shown.

CONTROL OF INFECTIOUS DISEASE

The control of infectious disease has baffled public health officers and school physicians in America for many years. It is also perplexing in France. Our bureau has a particularly interesting opportunity in this field in having turned over to it the children returning from Germany and Belgium to France through Evian. When the convoys are coming, two arrive each day, each consisting of approximately 600 refugees, from one-third to one-half of whom are children. Many of them have been exposed to the various infectious diseases and the problem of discovering such instances and of separating them from the others is exceedingly complex and difficult. The children are passed by one of our physicians and nurses shortly after they arrive, for a rapid inspection of glands, skin, throat and hair. The patients who are doubtful cases of infection are separated. When infectious disease is discovered, these patients are sent to a large hotel converted into a splendidly equipped hospital for isolation and treatment. After danger of infection is passed, they are either returned to their parents to move on to where they are to be permanently located, or, in certain instances, are sent on to convalescent homes or to other colonies.

In the hospital at Evian, a considerable number of cross-infections are always present, and there is a remarkable opportunity afforded to study the serious infectious diseases incident to childhood. We do not feel that we have solved the problem of preventing the spread of these communicable diseases to other parts of France. To do this would require colonization and isolation at Evian of all children during the period of incubation for the various infectious diseases. This may be advisable in the future, but has not been possible up to the present time. That many such cases are discovered and checked at Evian, and France, to this extent, protected from the spread of these contagions, is certain, and this contribution is greatly appreciated by the French. Certainly any American physician interested in the study of communicable disease should consider himself fortunate to have the opportunity of service at Evian. Dr. C. F. Gelston of San Francisco, has been largely responsible for the efficiency of the service.

TRAINING OF HEALTH NURSES

We realize, of course, that the American contribution to the French situation is largely a question of the development of nurses trained in public health methods. Americans cannot do this work. They can only assist a little in pointing out the way and with this end in view courses, some short, some longer, in the essentials of hygiene and public health nursing for children, have been instituted in connection with several hospitals and dispensaries. These courses have been attended by French women of fine ability, who apparently see the value of this sort of work. The courses have been arranged largely by Miss Harriet L. Leete, who is well known everywhere in America and who has had long experience in this field.

SCHOOL CANTEENS

In connection with our city dispensaries, the somewhat undernourished condition of many of the children seemed a striking feature. After investigation, it was found that many children received the principal meal of the day at the school canteens, and that this meal had been reduced in quantity because of war conditions. The American Red Cross has been able to add supplementary diet to these canteens in those *arrondissements* where it was most needed and in certain districts also outside of Paris. It has had a most happy result not only in improving the color and strength of the children but in affording an opportunity to demonstrate the good will of the American children in whose name this food was given to the thousands of French children who received it.

In addition to this increased nourishment given through the schools, quantities of food have been placed in the storerooms of several of the *mairies*, to be drawn on by our physicians and nurses for particular families where they find, after visiting and knowing their needs, that further diet is indicated. These added nourishments, offered under these unusual circumstances, has not only aroused a feeling of gratitude on the part of the French people, but has made possible an interesting study of the effect of diet in supplementing dispensary medical work.

The close connection which we always endeavor to emphasize between relief work for the civil population and the efficiency of the father or brother at the front, is emphasized by a postcard which our nurses carry with them and which is signed by the mother in the home, informing her representative in the fighting line that the American Red Cross nurses will care for their families in case of need.

GOVERNMENT ASSISTANCE

Perhaps no country in the world has such an elaborate system of allocations granted to dependent families, wives and children, dependent on the soldiers at the front. More than a reference to this subject would carry me far afield. There is much, however, which our own people can learn to great advantage from the French practice in this regard.

VALUE OF PROPAGANDA

American methods of propaganda in the field of child welfare have not been extensively employed in France. They seem to be received with unusual favor. General interest is being aroused by them in many parts of the country in all matters pertaining to the welfare of the child.

(*a*) *Exhibits in Large Cities.*—Two general plans are being followed: The organization of large exhibitions in child welfare in several of the large cities is undertaken. These exhibits resemble those we are familiar with in Baltimore, Philadelphia, Chicago, New York and elsewhere, but there is a novelty about them to the French which creates a feverish interest in the part of the attendants unknown at home. The story is told by wall-tablets, pamphlets, models, and driven home by lectures, practical demonstrations and the cinema and what was new in my experience, a very well arranged Punch and Judy show, in which the parents of the baby, after various vicissitudes, learned to care for it properly.

A cinema performance outside the exhibition building at Lyons I saw attended by a thousand people in a driving rain. Some of this interest may be due to the natural curiosity of the Latin race in any new thing, but much of it is real interest in the children of France and expresses a frank appreciation of the proffered help from America.

No one could see these eager people, so willing to adopt our suggestions, without a solemnizing sense of responsibility. Those of us who have aroused this interest must see to it that it is followed by placing at the disposal of every mother needing it, such help as is necessary to properly care for her children. It is difficult to overstate the opportunity which presents itself from this spontaneous popular response. At Lyons, where the first large exhibition is being held, Dr. Clifford G. Grulee of Chicago, who is director for that district, is fully alive to the importance of "follow-up" work, and is securing the cooperation of the various *oeuvres* of the city, and is beginning dispensary and social service work of his own, conducted in large part by French nurses who are taking the special training courses.

(*b*) *Smaller Exhibits in Rural Districts.*—Besides the large exhibition in the larger central cities, smaller exhibits in conjunction with the Rockefeller Commission are planned for the smaller towns and villages. Automobiles, designed to carry the panels and with a dynamo to run the lights for the cinema, are used. Every where, from the officials and people alike, the same cordial welcome awaits the representatives of the Americans in their effort to teach hygiene, as applied in the campaign against tuberculosis and infant mortality. In these smaller places, too, we endeavor to make use of the interest aroused by the organization of permanent activities in child welfare. Certainly the only limit to the lasting aid America can give to the children of France is the dulness of vision and the failure on the part of those of us who are privileged to be here, to grasp and develop this golden opportunity.

THE CARE OF DISPLACED POPULATION

The large number of refugees who are obliged to leave Northern France and seek temporary quarters elsewhere, present many problems in immediate and emergency relief, in which the American Red Cross is able to render splendid cooperative service. More than a million of these unfortunate people are being sent from the danger zone, in large colonies, to nearly all the other departments of France. Here they are met and cared for by sympathetic, intelligent delegates of the Bureau of Refugees and Relief, under Dr. Edward T. Devine of New York. The medical care of these people involves the organization of health centers, often the opening of temporary hospitals and the institution of other first aid measures, which not only greatly relieve the distressed people, but afford a wonderfully valuable experience in relief work to a group of Americans which should fit them, in an unprecedented manner, for effective emergency work of this kind at home.

JUVENILE DELINQUENCY

The amount of juvenile crime has increased greatly in France since the war. This has been true in all wars, when the head of the home has been removed, household discipline lessened and the family income reduced. I understand that the system of juvenile courts which, with probation officers and children's aid societies, have been so helpful in America in detecting early delinquency and in preventing its development, are not operative as yet in France. Here is a wonderfully attractive and useful opportunity for those who have the love of youth and expert knowledge which would yield returns past all computation for the long future.

SOCIAL SETTLEMENT

Some of us imagined that social settlements, as we have known them in England and America, were limited to these countries. We had not been in Paris long before we found several settlement houses fully equipped for social service ministering to needy districts. We have opened dispensaries for women and children in connection with these settlements and are learning at first hand that this form of social service is as useful here as at home. What a chance for a number of trained women to add to the corps and equipment of those who for so many years in comparative obscurity have been doing the pioneer work.

COMMENT

I have enumerated only a few of the things we can do to help this heroic, long suffering nation in the hour of her need, when the very doing of the job will enure to the lasting benefit of our own beloved land. Many of these opportunities have been seen and grasped by the honored Chief of the Children's Bureau, Dr. William Palmer Lucas of San Francisco, whose work it has been my privilege to share.

France has been fighting *our* battle for three long years. Our debt to her can never be paid. She offers us welcome to her shores, to her people; she opens to us her treasure house of statistical information; she presents to America, it often seems, her very soul, to make of it what we will. Surely this is a sacred task, a confidence which we will not abuse. Every one of us who has anything to contribute to the efficiency of our arms, to the comfort and upbuilding of the civilian population of France, must be eagerly willing to be used, assured that whatever of man power, of experience, of heart, of brains, we put into the right side of this world struggle, will not be lost, and more than that—it will live, take root and grow and it may become a tree whose leaves are for the healing of the nations. Only those who have ears to hear will heed this call.

THE MASSACHUSETTS CHILD CONSERVATION COMMITTEE: THE DETAILS OF ORGANIZATION AND WORK *

RICHARD M. SMITH, M.D.
BOSTON

Child conservation has become recognized so definitely as a part of the national war activity in foreign countries that no discussion of the importance of this work as a war measure is necessary. The Federal Children's Bureau with the endorsement of the President has designated this second year of the war as "children's year," and has published a program to be followed throughout the country. The method by which the work is to be accomplished is left to the various states to decide for themselves. Massachusetts has been working for the past year on child conservation. It seemed to me that it might be worth while to discuss at this time the methods employed, since they represent the distinctive feature of the work in each state.

ESTABLISHMENT OF COMMITTEES

On May 26, 1917, Dr. Allan J. McLaughlin, the Commissioner of Health, appointed from the Public Health Council, which is the advisory body of the state department of health, two members to serve with the director of the Division of Hygiene as a committee on child conservation. He also appointed an advisory committee of persons in the community particularly interested in children. The members of the committee are Drs. David L. Edsall, William J. Gallivan and Lyman A. Jones; of the advisory committee, Drs. Fritz B. Talbot, Robert L. De Normandie, Walter E. Fernald, William Healy, Richard M. Smith, Mrs. W. H. Lothrop, Miss Gertrude W. Peabody, and Miss Mary Beard. The distinction between the committee and its advisory members was never drawn sharply and from the first the two committees have met together and the actions of the joint body have been final. The advisory members have had equal authority with the members of the committee itself. This is an important detail as it indicates the spirit with which the work was undertaken by the officials of the department of health.

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* Submitted for publication Aug. 19, 1918.

* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

COOPERATION AFFORDED BY THE COMMISSIONER OF HEALTH

The commissioner at the beginning told the committee that he felt very strongly the urgency of child conservation particularly as a war measure and that he was anxious for the department of health to accomplish as much as possible in this part of its war work. He left the committee with a perfectly free hand to work out its plan of action and to put that plan in operation. At every stage the commissioner has been ready to give time, advice and encouragement and he has done everything in his power to put the machinery of the department at the disposal of the committee. Massachusetts owes an everlasting debt of gratitude to him for his farsightedness in recognizing the importance of child conservation and for his deeds which have made the work of the committee effective. A few weeks ago Dr. McLaughlin was called back into the public health service. Dr. Eugene R. Kelly, the new commissioner, is furthering the work started by his predecessor with uninterrupted interest and we are equally grateful to him.

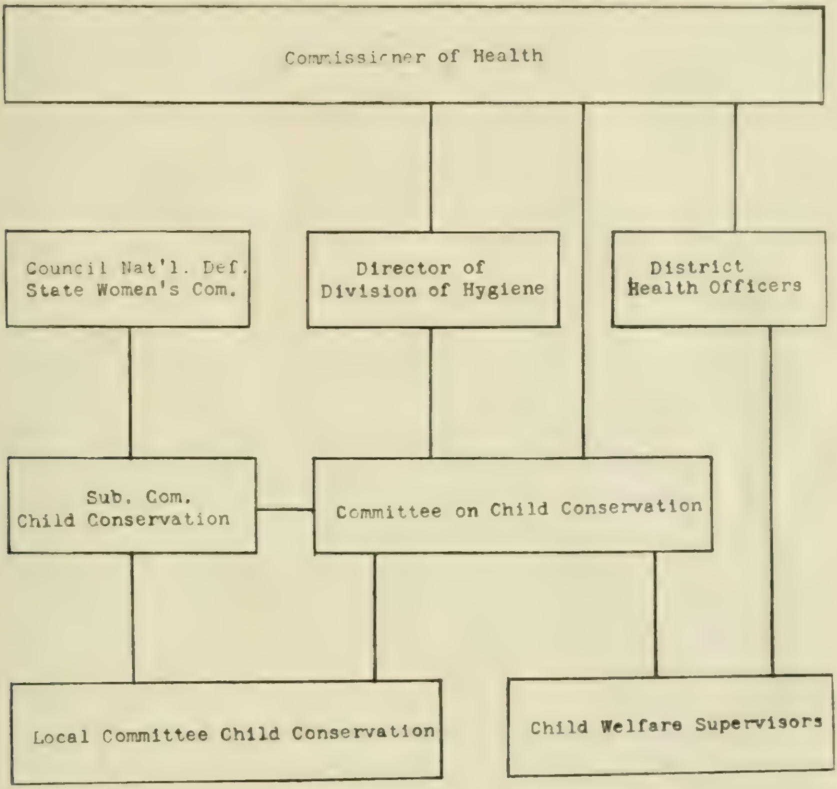
ADVANTAGES OF COOPERATION WITH THE CIVIL AUTHORITIES

This plan of doing child conservation work by a committee of the department of health has a certain advantage over the formation of a committee under some strictly war organization, as a public safety committee, in that it is in such close touch with the health department, and whatever is accomplished in tangible form may be embodied permanently in the machinery of the state department.

An important feature in the make-up of this committee is the combination of public officials and private individuals working together in a group which is more or less independent of all other groups and yet part of a state department. Many advisory committees have been formed in other connections, but this committee is in theory advisory, but, owing to the attitude of the commissioner, in fact, authoritative. The personnel of the committee is instructive as showing the variety of interest concerned and the different angles from which the questions are approached. There are two pediatrists, an obstetrician, a public health nurse, the superintendent of a state school for feebleminded, the physician in charge of the Boston Juvenile Court and the director of civilian relief of the New England division of the Red Cross. This is a medical committee and puts the responsibility for this work on us. Meetings of the committee have been held once a week since Aug. 1, 1917, and the attendance has been extremely regular.

EVIDENCE OF COOPERATION

A further evidence of cooperation is seen in the action of the women's department of the Council of National Defense. This department is represented in Massachusetts by a woman who is anxious that their child welfare work shall be in closest touch with the work of the State Committee. Therefore, she appointed as chairman of her Child Welfare Committee, Miss Mary Beard, who was already a member of our state committee, and as vice-chairman, Miss Gertrude Peabody, who has attended our meetings regularly and for all practical purposes has been a member of the committee. We have then on our state committee through its various individual members, representatives of the state health department, of the Red Cross, of the Council of National Defense and individual physicians in the community most interested in child conservation and having particular interest in special departments of that work.



Scheme of Organization of the Committee on Child Conservation

ORGANIZATION OF THE HEALTH DEPARTMENT

It is necessary to say a word about the organization of the Massachusetts Department of Health. The commissioner has under him eight district health officers who preside over the eight health districts into which the state is divided. In each of these health districts the health officer is practically a deputy commissioner, although all authority for work comes directly from the commissioner. For each one of these health districts the Child Conservation Committee appointed a public health nurse known as a Child Welfare Supervisor. These nurses were selected with the greatest care, and all of them had had not only public health training, but a considerable amount of experience in actual public health field work for children. It is hard to overstate the contribution made by these nurses. They have brought to the committee wonderful enthusiasm, expert knowledge, keen judgment and constructive suggestions. Without them the committee would have been able to do comparatively little. They are responsible directly to the committee but work in close touch with the district health officers. They are in fact introduced by them in the various communities to which they go.

SCOPE OF THE WORK

The first interest of the committee was to secure the facts in Massachusetts so far as child welfare work was concerned; to determine the number of children, the birth rate, the death rate and the facilities for taking care of children in each community. Therefore, we have made through these nurses surveys of the various cities and towns. To secure the facts the nurses have visited the representatives of the board of health, the child welfare agencies, the visiting nursing associations and other private or church societies which were doing child welfare work. They have received also first-hand information by personal investigation concerning the actual work being done by these organizations. From these facts the supervising nurses have made to the committee certain recommendations which seemed to them the desirable things to be done in that community for child conservation. The survey with the recommendations has been sent also by the nurses to the district health officers.

FREQUENT CONFERENCES HELD

Usually the nurses and the district health officers have discussed the situation together in conference. The district health officers have made whatever comments they saw fit on the surveys and on the recommendations and then have forwarded them to the commissioner of health. A copy of these letters and reports has been sent also to the committee. The committee has gone over in detail each survey with the nurses' recommendations and the district health officers' comments. The nurse who made the survey has been present at the meeting and frequently also the health officer of the district. The committee has adopted then certain recommendations which seem to them desirable in view of all the facts with reference to that particular community. The secretary of the committee then has written to the community a letter stating the recommendations and urging that efforts be made to carry them out and offering the advice and help of the committee to that end. The commissioner of health at the same time has written a letter to the local board of health in that town or city calling attention to the fact that the survey has been made, sending him a copy of the statement of facts and of the recommendations which have been made by the committee and urging that the local board of health do everything it can to help put the plan into operation.

SUGGESTIONS MADE FOR IMPROVING THE WORK

In the recommendations of the committee and the commissioner we have called sometimes for an extension of the work of the local department of health, sometimes for the addition of more nurses by the Visiting Nursing Association, and sometimes for the providing of free obstetrical beds in hospitals. Almost invariably we have urged more prenatal work, either by the addition of prenatal clinics or the extension of nursing service, and also invariably for the supervision of well children from birth up to 5 years of age, and not infrequently in connection with this the establishment of well baby clinics. We have asked also that outpatient departments be established to which sick children could be brought for treatment and sometimes that a children's ward be built in connection with a general hospital. We have endeavored to see that prenatal care, good obstetrical care and postnatal care from birth up to 5 years of age is provided for every child.

PUBLIC HEALTH TRAINING FOR NURSES

We have insisted everywhere on the necessity of public health training for nurses doing this work. The secretary early last year wrote a letter to the State Nursing Association urging them to impress on all the nursing organizations of the state the importance of keeping the standard of public health nursing high.

PUBLICITY AN IMPORTANT ADJUNCT FOR SUCCESSFUL RESULTS

We have tried further to stimulate local publicity both for the raising of funds to carry on the work and for the awakening of interest in the importance of child conservation. We have had a person giving half time to directing newspaper publicity. Also many public meetings have been arranged at which talks have been given. Members of the committee have spoken at twenty-three such meetings and the supervisors at 136 meetings. We have reached at least 10,000 people by this means.

CONCENTRATION BECAME NECESSARY

When the committee first started we tried to include all parts of the child conservation program, that is, infant care, school hygiene, juvenile delinquency, child labor, day nurseries, and similar agencies. We found, however, that this was such a large program that our energies would be too scattered unless we localized our efforts. We decided that for the first year we would receive the largest return by concentrating on the care of the child up to school age. We have digressed from the usual procedure, however, in many instances, and have made special recommendations which seemed to be urgent in a particular locality. For instance, in some cities the day nursery situation was acute, and we have aroused the local community through our supervisors to take action in the matter. We hope later to study this whole subject in a broader way with the possibility of legislative standardization.

ILLEGITIMACY AND VENEREAL DISEASE

We have been interested in the question of venereal disease and illegitimacy as it affects children and is made of particular importance by the war. The Massachusetts State Department of Health has this year made syphilis and gonorrhea reportable diseases and in this connection has started a very active campaign of general education. Our committee has been cooperative so far as we could be in this plan, but the work of the department of health has made it unnecessary for us to act independently in this particular.

DELINQUENCY IN CHILDREN

The question of juvenile delinquency is now becoming, because of the war, a definite increasing factor in child conservation work. We are doing already what we can to collect facts regarding it. We hope later to make definite recommendations for its control.

CARE OF THE OLDER CHILDREN

The care of the school child in the larger cities is a big enough study to demand an independent investigation, and we have not considered it there? In the smaller communities, however, the number of schoolchildren is not large and is intimately connected with the other parts of public health work. In these places we have made specific recommendations with reference to school nursing, dental care, preventive and follow-up work.

LOCAL COMMITTEES ON CHILD WELFARE ESTABLISHED

A very important feature of the state work has been the formation of local committees. The child welfare vice-chairman of the women's department of the Council of National Defense, Miss Peabody, working with the child welfare supervisors, has organized in the various cities and towns of the state local committees on child welfare. These committees have for the most part been independent of any local organizations except for the Women's Council of National Defense, and have included in their membership representatives of the local boards of health, of the local physicians and of agencies interested in child welfare. We have found that by creating this independent body it has been possible to bring together many persons and organizations which formerly had been working at cross-purposes or in actual opposition.

COOPERATION THE SECRET OF EFFICIENCY

Whatever success has been attained in Massachusetts has been due in no small measure to the efficiency of this part of the work. Miss Peabody has given practically her entire time since September to this and has gone all over the state organizing the local committees. Up to date 183 such committees have been formed. There have been held several large meetings in Boston and elsewhere during the year by the chairmen of these local committees. At these meetings questions of policy and method are discussed and a great deal of enthusiasm fostered. It is to these committees that the recommendations from the state committee are sent. There are still a few towns under 6,000 inhabitants where local chairmen have not yet been appointed, and there are a good many rural communities in which practically no work has been done. It was impossible to make surveys of these rural communities during the winter, but we hope this summer to do something toward arousing interest in child welfare and in working out a plan of action for them.

KEEPING A RECORD OF RESULTS

The recording of results is difficult. Organized child welfare work is not new in Massachusetts. The department of health has been working on child conservation, and some local committees have been doing effective work for many years. The seeds of our work the last year, therefore, have fallen on ground already partly prepared. Often the work of the state committee has served largely to crystallize sentiment on the need of this work and has helped the local boards of health or private organizations to accomplish things which had been desired for a long time. But in some places nothing at all had been done for children and the local health officials had given no thought to the matter. Here we worked on virgin soil. In almost every instance throughout the state the suggestions made to the local boards of health and to the private organizations and individuals have been received with enthusiasm. A spirit of cooperation hard to overcommend has been manifested by everybody. All have worked together for the benefit of the children. Much more has been accomplished than it is possible to record in figures because of the statewide interest that is now manifest in child conservation. The activities of the local committees are now so great that our difficulty at present is to keep in touch with all that is being done and to give the assistance which is constantly being asked.

We know, thus far, that thirty-one new public health nurses are to be employed by the boards of health and private organizations to do child welfare work. Some of these are already at work. Eleven new infant welfare stations have been opened in six cities and nine prenatal clinics opened in six cities. A considerable number of others are to be opened in the near future. A free bed has been secured in one hospital to be at the disposal of the Child Welfare Association in that city to use for cases needing hospital care. Several new organizations for child welfare have been formed — one in a locality where previously nothing had been done in any kind of public health work. The nursing personnel has been changed in several places with the appointment of trained public health nurses. In two cities we have loaned one of the supervisors to take charge at the beginning to direct this reorganization. Approximately $50,000 has been provided since Jan. 1, 1918, for new child welfare work.

General interest has been aroused in the care of the child from one to 5 years of age. Most of the infant welfare associations are extending their work to include this period.

RESULTS OF THE YEAR'S WORK

This year's work in Massachusetts has demonstrated two things which have an application quite beyond the limits of the state. (*a*) A workable method of cooperation between public officials and private organizations and individuals. This method requires for success an appreciative spirit in the public officials for the enthusiasm and desire for results inherent in private workers, and a tolerant sympathy on the part of the layman for the necessary conservatism of official action. (*b*) The universally favorable response which comes from every community when an opportunity is presented for constructive and definite work for children.

During the year we have found many interesting facts of a technical nature which may be reported on at a later date.

The form of survey and scheme of organization is appended.

329 Beacon Street.

FORM OF SURVEY

I.

Name of city or town.
Area:
Population:
Chief nationalities:
Industries:
Number of births for................ Birth rate:
Number of deaths under 1 year...... Infant mortality rate:
Number of deaths between 1 and 5 years........
Department of health:
Prenatal work:
Baby welfare work:
Supervision of child of preschool age:
Other nursing agencies:
Hospitals:
Other child saving agencies:

II.

Housing conditions:
Water:
Milk:
Schools:
Factories:
Garbage:

III.

Deaths by ages
1 day and less.
1 day to 1 week.
1 week to 1 month.
1 month to 2 months.
2 months to 3 months.
3 months to 4 months.
4 months to 5 months.
5 months to 6 months.
6 months to 7 months.

Deaths by ages
7 months to 8 months.
8 months to 9 months.
9 months to 10 months.
10 months to 11 months.
11 months to 12 months.
1 year to 2 years.
2 years to 3 years.
3 years to 4 years.
4 years to 5 years.

Seasonal distribution of deaths: Under 1 year. One to 5 years.

Causes of death: Under 1 year. One to 5 years.
Congenital
Respiratory
Intestinal, etc.

Deaths by nationality—using birthplace of mother:

Maternal deaths:
Cause. At home or hospital Physician or midwife.

IV. Notes:
Comments by nurse on local situation.

V. Recommendations:

A CONSIDERATION OF THE ETIOLOGY OF PHLYCTENULAR DISEASE OF THE EYE *

HOWARD F. HANSELL, M.D.
PHILADELPHIA

The study of etiology of phlyctenular disease of the eye is instructive to the internist and to the oculist. The opinion is almost universal that the repeated formation of phlyctenules is a manifestation of tuberculosis. The character of the corneal involvement in systemic disease or focal infection varies according to individual idiosyncrasy and, while we can readily accept in some patients the tubercular origin, in others we cannot, or, if the dyscrasia should be tubercular the corneal disease may take other forms, such as sclerosing keratitis, numerous fine points of infiltration, keratitis secondary to iritis, or lupus.

ETIOLOGIC FACTORS

The published evidence for the tubercular origin of phlyctenular disease is strong. Goldbeck[1] studied thirty-nine cases thoroughly and systematically. Some of his conclusions are worthy of thoughtful consideration.

Predisposing Causes.—The nodular cellular lymphoid deposits (phlyctenules) are local eye manifestations of a constitutional dyscrasia strongly suggestive of tuberculosis—if not tuberculosis— then something very closely associated bearing a striking resemblance in its symptomology to tuberculosis. Of the thirty-nine patients, seven had phthsisis, sixteen had some form of tuberculosis, as cervical adenitis or tuberculous bones, thirty-two had a positive von Pirquet reaction, eighteen adenoids and diseased tonsils. The tubercle bacillus was found six times in microscopic sections.

We must not expect to find signs of active tuberculosis in the lungs or elsewhere in the body in many of the cases. That they may be present is shown by Goldback and others. Phlyctenulosis may be an early symptom in attenuated form or, as described by Wirtz,[2] a secondary or even tertiary form. He investigated twenty-one cases of "rheumatic" eye affections, for example, episcleritis, uveitis, sclerokeratitis, some with and some without tertiary tuberculosis (disease of the glands and bones). In twelve cases there was no sign of active tuberculosis. The patients were all suffering or had suffered from articular "rheumatism" so called. In every one of these cases he found tubercle bacilli in the blood.

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* Submitted for publication July 20, 1918.

[1] Goldback, L. J.: Lymphatic-nodular Keratoconjunctivitis (Phlyctenules), Tr. Sect. on Ophth., Am. Med. Assn., 1917, p. 286.

[2] Wirtz, R.: Ueber Beziehungen der rheumat. Augenerk. zur "sekundären" Tuberkulose, Klin. Monatsb. f. Augenh., 1913, **15,** 607.

The majority of cases of ocular phlyctenulosis occur in children or young adults. If we accept the attenuated tuberculosis theory—secondary and tertiary—we must admit that such cases come under those headings.

The scrofulosis of the older authors presents clinically exactly the same appearances. The two affections are doubtless identical in tubercular subjects. Other cases, again, are found in individuals who, as far as can be ascertained by laboratory and clinical methods, are free from tuberculosis. In them, presumably, attenuated syphilis is the underlying dyscrasia.

Exciting Causes.—The immediate or exciting causes are various. They may be intestinal irritation, nasal disease, indigestible food, dental irritation, intestinal worms, and similar conditions. Repeatedly, I have found coincident inflammation of the nasal mucous membrane, adenoids and enlarged tonsils associated with phlyctenulosis. Again, the administration of an effective anthelmintic has been followed in the course of one or two days by complete clearing up of the ocular inflammation. My experience has led me to believe that the subjects of phlyctenules are, as a rule, poorly nourished, overfed, underfed, or misfed children of poor and ignorant parents, living in the midst of unsanitary surroundings, and may well often be the victims of attenuated tuberculosis or syphilis.

That reflex irritation from the teeth may cause phlyctenules is well illustrated by the following case recently reported in *The Journal of the American Medical Association.*

> The patient was a girl of 11 who had been under constant treatment for sixteen months. Every known method of treatment was earnestly tried but without success. Corneal phlyctenules would appear and pass through the process of ulceration and cicatrization absolutely uninfluenced by any local or systemic measure. Extraction of an infected right lower molar resulted in a prompt disappearance of the hitherto incurable photophobia and the cessation of the phlyctenular process. There has been no return within the past year.

COMMENT

Such cases as this, and they are not infrequent, indicate the importance of seeking the active cause whether or not the patient may eventually become tuberculous.

The most recent support of the tuberculous origin of phlyctenulosis is a paper by Gibson.[3] The abstract is here given.[4]

> Clinical observations in ninety-two cases of phlyctenular conjunctivitis revealed the presence of tuberculosis in ninety cases, as shown by a positive von Pirquet test. In the two giving a negative reaction, the diagnosis was doubtful. No other condition, either local or general, could be found with sufficient frequency even to suggest any direct influence in producing the disease. Phlyctenules were produced experimentally in tuberculous rabbits in eight instances; six times as a complication of a conjunctival reaction resulting from the instillation of tuberculin, twice in the absence of local irritation of any kind. Numerous attempts to produce the condition in animals not tuberculous were unsuccessful. The pathology of the experimental lesions was similar to that of human phlyctenules. The microscopic findings suggested a tuberculosis origin.

CONCLUSIONS

Gibson is convinced that all clinical, experimental and pathologic evidence points to tuberculosis, and tuberculosis alone, as the cause of phlyctenular disease. Most clinicians will not agree with this sweeping statement. Too many cures have been effected by other remedies to permit the acceptance of only one cause or one dyscrasia. A single attack rapidly recovered from by the use of local remedies does not point to tuberculosis. Repeated attacks occurring in a patient who is "scrofulous," that is, presenting the signs of remote syphilis or tuberculosis, clearly indicate a grave underlying dyscrasia.

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[3] Gibson, W. S.: The Etiology of Phlyctenular Conjunctivitis, Am. Jour. Dis. Child., 1918, **15,** 81.

[4] Abstracted in the Jour. Am. Med. Assn., 1918, **70,** 8.

IS THE AMOUNT OF CALCIUM USUALLY GIVEN IN DILUTIONS OF COW'S MILK INJURIOUS TO INFANTS?*

A REPLY TO HOLT, COURTNEY AND FALES

A. W. BOSWORTH, A.M., H. I. BOWDITCH, M.D.
AND
LOUISE A. GIBLIN, B.S.
BOSTON

In the July, 1918, issue of the American Journal of Diseases of Children, Holt, Courtney and Fales reply to a paper by us, which appeared in the June issue of the same journal, in which we presented some studies on "Calcium in its Relation to the Absorption of Fatty Acids." Their reply was prompted by a "desire to present some conclusions drawn from results obtained in this laboratory which may perhaps allay the fears of calcium injury from the use of simple dilutions of cow's milk in infant feeding." As the conclusions drawn by them were from results obtained from entirely different types of cases than those studied by us, we feel constrained to reply. They say:

> The position is taken that this special milk provides an improved form of feeding over simple cow's milk because on the latter children suffer a serious loss of fat through the excretions of soap stools, also that there follows from such feeding excessive constipation, leading frequently to a general upset, termed by the authors a "blowup."

Nowhere in our article have we taken the position that our reconstructed milk provides "an improved form of feeding" over simple cow's milk *except for the type of cases under discussion in that article.* Nowhere in our paper have we stated that children suffer a serious loss of fat through the excretion of soap stools as a result of such feeding, although we believe such might be the case in the type of cases mentioned in our article. Nowhere in our paper have we made a general statement that the feeding of simple dilutions of cow's milk results in excessive constipation. We have said that such feeding of cow's milk often causes severe constipation, and have taken a few such cases for study. Nowhere in our article have we said that such constipation will lead "frequently to a general upset" except in the special type of case under discussion in that article.

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They discuss our article under three headings, and we wish to reply in the same manner.

1. Is there a serious loss of fat (otherwise than through diarrhea) when the simple dilutions of cow's milk are fed?

In criticizing our results they present data from "a group of thirty-two children from 2 to 15 months of age," and they say that "among the stools from the thirty-two children before mentioned there was only one which from its appearance could be called constipated."

In our article we specifically said, "We have collected a number of the firm, characteristic soap stools usually eliminated by infants receiving modified cow's milk, such infants as are often constipated and frequently show marked distention of the bowels due to the accumulation of gas."

It is obviously unfair for Holt, Courtney and Fales to select thirty-two children, only one of whom showed signs of constipation, and compare data obtained from them with data secured by us from the study of twenty-three infants, all of which showed distinct signs of constipation and disturbances in their fat metabolism, and some of which could not tolerate any simpler milk dilution containing fat. For this reason the figures given in their "Table 1.—Comparison of figures for fat retention," have no bearing on the matter whatever.

They also assume that we claim that only the soluble calcium in cow's milk is available for soap formation, ignoring entirely our distinct demonstration that the calcium combined with casein is also available for soap formation.

They also say, "The inference that a high calcium intake causes a serious loss of fat, does not seem to be warranted." In reply we can only say that we do not feel that we have drawn any such inference, although such inference might have been drawn, with reference to the special type of case considered in our article, from the data given in our Table 2.

In order to show that the presence of a considerable portion of calcium soap in stools cannot be called an abnormality if breast fed infants are to be taken as a standard, they present the following:

> "In one case in which an exact record of the intake of breast milk was obtainable the following results were found. With an intake of 41.9 gm. of fat, the total fat excretion was 2.26 gm., of which 63.8 per cent. was soap. The fat retention was 94.6 per cent. of the intake. The calcium intake was 0.355 gm. This child was at the time doing extremely well and has continued to do so. In this baby with a small calcium intake, practically the same results were found as with many bottle-fed infants with two or three times the calcium intake. *This child had for its age (about 1 month) an unusually large fat intake.*"

The italics are ours and they seem to us to explain why this child excreted 2.26 gm. fat. Had this child been given an average quantity of fat, we presume the total fat excretion would have been lower, probably about 1 gm. Had a large number of babies receiving an average amount of fat been examined, and the same results obtained, their point would have had more weight.

2. Is there danger of constipation with serious consequences in infants fed on simple dilutions of cow's milk?

Under this heading they present no data to show whether or not there is danger of constipation from such use of cow's milk. They discuss the data secured by them from the thirty-two infants mentioned before, only one of which showed any signs of constipation. From this discussion they draw the conclusion that the total loss of fat is very seldom, if ever, of serious consequence, a question which is not touched on by us in our paper; and they advance the statement that "A tendency to constipation in infants receiving simple cow's milk dilutions is generally controlled without great difficulty."

We can only reply by saying that there is danger of constipation with serious consequences when certain types of infants are fed simple dilutions of cow's milk, and that these infants have done well on our reconstructed milk.

3. May there not be a danger in too low a calcium intake?

There certainly can be danger in too low a calcium intake, but very fortunately we are able to control the amount and form of calcium which enters into our reconstructed milk. The figure given in our article for the amount of calcium in our reconstructed milk is "0.009 per cent., or more if desired." The figure 0.009 per cent. represents the minimum percentage of calcium obtainable and does not by any means imply that 0.009 per cent. of calcium is the amount present in our finished product.

We quote the last paragraph of their paper:

> In conclusion, we believe it is yet to be demonstrated that infants fed on simple dilutions of cow's milk do not retain an adequate amount of fat when the stools are formed or semiformed and soapy, nor do we think that a high calcium intake necessarily causes a large fat loss in the feces; while a great reduction of the calcium in the food of infants may be attended with considerable risk.

These generalized conclusions drawn by Holt, Courtney and Fales from the data presented by us in fair criticism seem to demand a prompt reply, for in our paper we confined ourselves to a study of a specific type of case and we refrained from drawing general conclusions until we have presented further data which we hope to incorporate in subsequent articles.

THE BEARING OF CUTANEOUS HYPERSENSITIVENESS ON THE PATHOGENICITY OF THE BACILLUS ABORTUS BOVINUS *

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It is not the purpose of this paper to enter into an exhaustive résumé of the literature pertaining to cutaneous hypersensitiveness, nor to discuss the various theories that have been offered as an explanation of its occurrence. With the exception of a very few observers who explain the phenomenon as an indication of immunity or a phase of anaphylaxis, cutaneous hypersensitiveness is now generally considered to be an evidence of infection, although it is by no means certain that the future will not modify some of the generally accepted views referable to the methods of its production.

In an effort to determine the frequency with which certified milk was infected with tubercle bacilli, in 1916 and 1917, a large number of guinea-pigs was injected with the sediment of this product and the animals studied in the following manner. Several weeks after the milk was injected intradermal tests were made. At this time blood was taken from the heart for agglutination determinations. The animals were later chloroformed and in addition to a careful pathologic study of all the viscera, attempts were made to isolate the invading organisms. The milk invariably produced in the infected animals a chronic disease simulating tuberculosis, but which did not kill the animals, and whose lesions corresponded exactly with those so frequently described as produced in guinea-pigs by the *Bacillus abortus bovinus.*

DIAGNOSTIC TESTS

Of the various diagnostic tests employed, none was as constantly positive as the intradermal test. Of thirty guinea-pigs that showed lesions following milk injections, this test was positive in 100 per cent. of the animals. The characteristics of the reaction were marked induration, frequently with central necrosis, an area of at least 1 cm. in diameter with persistency of the reaction over the forty-eighth hour. Six animals used as controls gave negative tests. Of eight

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guinea-pigs that were inoculated from a culture recovered from the spleen of one of the infected animals, 100 per cent. of the animals showing lesions gave positive intradermal tests. Two controls gave negative reactions. Four guinea-pigs were inoculated with a macerated spleen, that showed characteristic lesions, and 100 per cent. gave positive intradermal tests and typical lesions. Four controls were negative. A series of ten guinea-pigs, that had been injected with tuberculous material of various types, was likewise used as a control, and in this group, whereas every one gave a positive intradermal test when tuberculin was used as an antigen, when abortin was used all tests were negative. To study the value of the intradermal test in chronic bacillus abortus infections, a series of thirty guinea-pigs, that had been injected intraperitoneally with polyvalent cultures of bacillus abortus about one year before, were tested, and in 100 per cent. of the animals that on postmortem showed characteristic lesions of abortus disease, positive intradermal reactions were obtained. The controls were invariably negative. The striking result of these experiments is that cutaneous hypersensitiveness as evidenced by positive intradermal tests in guinea-pigs is an absolutely positive sign of infection by the *B. abortus bovinus*. This fact is equally true whether the disease is acute or chronic in character.

PATHOGENICITY

The evidence that has been gathered during the past few years relative to the pathogenicity of the *B. abortus bovinus* for infants has not been very conclusive. The reasons for this are evident. First, only a few workers have interested themselves in the subject, and secondly, they have confined their experiments to an investigation of complement fixation and agglutination reactions. Whereas Sedgwick and Larson obtained some excellent results working along these lines, and although it may be conceded that positive agglutination and complement fixation tests suggest the possibility of human infection with the *B. abortus bovinus,* one must remember that either active or passive immunity to the organism will give similar reactions.

With the fact established that raw milk contains large numbers of abortus bacilli, and that children fed on this milk develop antibodies in their serum, track must not be lost of the conclusion that has been reached by numerous workers, that the milk likewise contains antibodies which may pass through the intestinal mucosa into the blood, establishing a passive immunity that will give positive complement fixation and agglutination tests. In the above mentioned experiments, in all of which positive intradermal reactions were obtained only when the animals were infected, positive agglutination reactions were also present in dilutions from 1 : 600 to 1 : 1,000, and sometimes in dilutions greater than 1 : 2,000. Realizing that in this series of investigations, positive intradermal tests were always a sign of infection, and that in these infections agglutination reactions were likewise positive, and further appreciating that antibodies giving positive agglutination reactions might be present in the serum of animals due to passive immunity without infection, a series of experiments was devised to prove, if possible, (1) that antibodies could be produced in the blood of guinea-pigs, that would give positive agglutination reactions in the absence of infection, and (2) if these antibodies were produced in the absence of infection, whether or not cutaneous hypersensitiveness was present.

EXPERIMENTS

Experiment 1.—Ten guinea-pigs were injected Oct. 23, 1917, intraperitoneally with 1,000 million dead bacillus abortus consisting of a polyvalent mixture of cultures that were obtained from the animals that had been previously injected with certified milk, killed by heating to 60 degrees for half an hour, to which 0.3 per cent. tricresol was added. A second injection of 2,000 million was given Oct. 31, 1917, and a third injection of 4,000 million Nov. 24, 1917. Intradermal tests were made five, ten, fifteen and twenty days after the last injections using as antigens bacillus abortus protein, 1 : 1,000; bacillus abortus broth, 1 : 3; bacillus typhosus protein, 1 : 1,000 and tuberculin, 5 per cent. solution, 2½ per cent. human and 2½ per cent. bovine. The bacillus abortus protein was prepared as follows: A saline suspension of living organisms grown on peptic digest agar was precipitated by absolute alcohol, centrifuged, the supernatant alcohol decanted and reprecipitated with absolute alcohol, alcohol again decanted and precipitate treated twice with ether, centrifuged and ether decanted; dried rapidly with current of air, then dried in the desiccator to a constant weight and kept in the desiccator The abortus broth consisted of from fifteen to twenty cultures grown in glucose broth for eight weeks, then killed by heating to 100 degrees for one hour, after which 0.3 per cent. tricresol was added. The tuberculin used was a 5 per cent. solution of alcoholic precipitated O. T. in 0.3 per cent. tricresol. The bacillus typhosus protein was prepared by the same method as the bacillus abortus protein. All of the intradermal tests were negative corresponding to the results obtained with two normal guinea-pigs. Agglutination reactions were positive in rather stronger dilutions than in the animals that had been infected with the milk. On May 6, 1918, about six months after the last injection, these animals were again injected intraperitoneally with 4,000 million bacillus abortus killed and intradermal tests made ten and twenty days afterward, using the same antigens. The results were again absolutely negative with respect to cutaneous hypersensitiveness. Several of these animals were killed with negative postmortem findings.

Experiment 2.—Ten guinea-pigs were injected Oct. 23, 1917, intraperitoneally with 500 million bacillus typhosus, a polyvalent vaccine killed by heating to 56 degrees for half an hour to which 0.3 per cent. tricresol was added. A second injection of 1,000 million was given Oct. 31, 1917, and a third injection of 2,000 million Nov. 24, 1917. Intradermal tests were made five, ten, fifteen and twenty days after the last injection, using the same antigens as in Experiment 1. All of the tests were negative. Agglutination tests run at the same time were positive in dilutions of 1 : 2,000. On May 6, 1918 six months after the last injection, these animals were again injected intraperitoneally with 2,000 million bacillus typhosus vaccine, and intradermal tests were made ten and twenty days later with negative results. Several of these animals were chloroformed and nothing pathologic was found.

Experiment 3.—Ten guinea-pigs were injected intraperitoneally Oct. 23, 1917, with 1 c.c. of a 1 per cent. solution O. T. bovine. A second injection of 1 c.c. of a 1 per cent. solution was given on Nov. 26, 1917. Intradermal tests were made five, ten, sixteen and twenty-two days after the last injection, and all were negative corresponding to two controls. On May 6, 1918, about six months after the last injection, 1 c.c. of a 1 per cent. solution of O. T. was again injected and intradermal tests made ten and twenty days later with likewise negative results. Complement fixation tests on the serum of these animals, using the tubercle bacillus as an antigen, were negative. Several were killed, and the postmortem findings were negative.

Experiment 4.—Ten guinea-pigs were injected Oct. 24, 1917, intraperitoneally with 1 c.c. of a 0.5 per cent. solution of bacillus abortus protein prepared according to the technic previously described in connection with the preparation of the antigens used for the intradermal tests. A second injection of 1 c.c. of a 0.5 per cent. solution was given intraperitoneally Nov. 26, 1917. Intradermal tests were made five, ten, sixteen and twenty-two days after the last injection and all were negative. On May 6, 1918, about six months after the last injection, 1 c.c. of a 0.5 per cent. solution of bacillus abortus protein was again injected intraperitoneally, and there were no positive results. Positive agglutination reactions were obtained with these animals, and necropsies revealed no evidence of abortion disease.

In view of the very definite absence of cutaneous hypersensitiveness in this group of experiments, it was deemed advisable to repeat the series with more intensive immunization.

Experiment 5.—Ten guinea-pigs were injected intraperitoneally Jan. 24, 1918, with 500 million bacillus typhosus vaccine. A second injection of 1,000 million was given on Feb. 9, 1918; a third of 2,000 million on Feb. 26, 1918; a fourth of 1,000 million on May 8, 1918; a fifth of 1,000 million on May 11, 1918, and a sixth of 1,000 million on May 13, 1918. Intradermal tests were made ten days after the last injection and all were negative. The same antigens were used as in the previous set of experiments with the addition of bacillus paratyphosus protein prepared similarly to the bacillus abortus protein.

Experiment 6.—Ten guinea-pigs were injected intraperitoneally Jan. 24, 1918, with 1 c.c. of a 1 per cent. solution of O. T. bovine. A second injection of 1 c.c. of a 2 per cent. solution was given on Feb. 9, 1918; a third of 1 c.c. of a 2 per cent. solution Feb. 25, 1918; a fourth of 1 c.c. of a 2 per cent. solution on May 8, 1918; a fifth of 1 c.c. of a 2 per cent. solution on May 11, 1918, and a sixth injection was given on May 13, 1918, of 1 c.c. of a 2 per cent. solution. Intradermal tests made ten days after the last injection were negative. Postmortem examinations were negative.

Experiment 7.—Ten guinea-pigs were injected intraperitoneally Jan. 24, 1918, with 1,000 million dead bacillus abortus prepared as in Experiment 1. On Feb. 9, 1918, 2,000 million were given intraperitoneally; on Feb. 25, 1918, 4,000 million; May 8, 1918, 1,000 million; May 11, 1918, 2,000 million, and May 13, 1918, 2,000 million; a total of six injections with 12,000 million killed bacteria. Intradermal tests ten days after the last injection were negative. Postmortem examination revealed nothing abnormal.

Experiment 8.—Injected ten guinea-pigs intraperitoneally with bacillus abortus protein prepared as previously described. On Jan. 24, 1918, 1 c.c. of a 0.5 per cent. was used; Feb. 9, 1918, 1 c.c. of a 1 per cent. solution; Feb. 25, 1918, 1 c.c. of a 2 per cent. solution; May 8, 1918, 1 c.c. of a 0.5 per cent. solution; May 11, 1918, 1 c.c. of a 0.5 per cent. solution, and May 13, 1918, 1 c.c. of a 0.5 per cent. solution; six injections in all. Ten days after the last injection, intradermal tests were made and all were negative. Postmortem examinations showed no lesions.

Experiment 9.—Ten guinea-pigs were injected intraperitoneally with dead bacillus paratyphosus San Antonio guinea-pig strain, the injections taking place, 500 million, Feb. 9, 1918; 1,000 million, Feb. 26, 1918; 1,000 million, May 14, 1918, and 1,000 million May 16, 1918. Intradermal reactions were made ten days after the last injection, and all were negative. Agglutination reactions have not been completed in this group.

COMMENT

A careful analysis of these experiments suggests some very interesting conclusions. In the first place, in all of the guinea-pigs that were inoculated with milk, those animals showing on postmortem examination characteristic lesions of abortion disease gave striking evidence of cutaneous hypersensitiveness and likewise positive agglutination reactions. Similarly, those animals injected with cultures of bacillus abortus, that developed lesions, gave marked intradermal reactions and positive agglutination tests. Controls, on the other hand, which consisted of two different types of animals, first, those whose resistance prevented them from developing the disease, and second, normal animals failed absolutely to give either positive intradermal tests or agglutination tests.

In contrast to this set of experiments, in a series of animals that had been intensively immunized by the intraperitoneal injection of dead *B. abortus bovinus* or bacillus abortus protein, in no single instance was cutaneous hypersensitiveness present, although agglutination reactions were usually positive, perhaps a trifle less marked than in the infected animals. Particular emphasis has been laid in this paper on the experiments which dealt with the abortus bacillus because it was this phase of the problem that started the investigation.

Drawing an analogy from these experiments, it seemed reasonable to assume that the previous work that had been done in connection with the serums of infants fed on raw milk, and which showed positive complement fixation and agglutination tests, might be an evidence of either infection or immunity, and if it was an evidence of infection that cutaneous hypersensitiveness should be present. This deduction was based largely on the one other chronic disease to which children are heir, namely, tuberculosis. Krause and others have shown that intradermal tests are always present when there is a definite infection, and this same observation has been made by numerous laboratory workers in connection with tuberculosis of guinea-pigs.

FURTHER TESTS

Accordingly, a series of infants was selected in hospital and ambulatory practice, all of whom were receiving raw milk, either certified or inspected, and they were tested in the following manner:

Bacillus abortus protein was prepared as previously described and suspended in saline containing 0.5 per cent. phenol. After trying out a number of different solutions to determine the most satisfactory dosage, it was decided to give

0.1 c.c. equaling 1/500 mg. As a control, the same dosage of bacillus typhosus protein was used.

Seventy-five infants were tested, and with two exceptions, in no single instance was there any evidence of cutaneous hypersensitiveness. A brief consideration of these two exceptions is more than interesting. They were young children about 2 years of age, who had been suffering for several months from chronic bone tuberculosis. The reaction to the typhoidin in both cases was greater than the reaction to the abortin, the test in the typhoidin control being 1.5 cm. in diameter, while the abortin reaction measured only 1 cm. These two positive reactions probably represent a phase of cutaneous hypersensitiveness that is being more or less generally discussed at the present time, namely, that element of the reaction which represents a type of sensitization common to the vegetable protein in all bacteria. It is thoroughly logical, therefore, to assume that these positive tests represented simply the effect of the long standing infection by the tubercle bacillus, and were in no sense specific. This is more readily appreciated when one considers that the typhoidin reaction in both of these children was more pronounced than the abortin reaction. A further consideration of this phase of cutaneous hypersensitiveness will be discussed in a subsequent paper.

CONCLUSIONS

1. In guinea-pigs, infection with the *Bacillus abortus bovinus* always produces cutaneous hypersensitiveness.

2. In guinea-pigs, tuberculosis, which is the disease that the lesions of abortus infection most closely simulate, always gives cutaneous hypersensitiveness.

3. In infants, infection with the tubercle bacillus, with a few exceptions that are familiar to every one, gives marked cutaneous hypersensitiveness.

4. Inasmuch as these two diseases behave so closely as to both character of lesions and cutaneous hypersensitiveness in guinea-pigs, one might expect a similar condition in infants if abortion disease were present, considering that tuberculosis gives in man the same lesions and the same skin reactions as in animals.

5. In a series of seventy-five infants fed on a high bacillus abortus containing milk, cutaneous hypersensitiveness was not present.

6. With the evidence from guinea-pig experimentation indicating that cutaneous hypersensitiveness is always present in acute or chronic abortion disease, the constant absence of this phenomenon in infancy is strikingly suggestive that the *Bacillus abortus bovinus* is not pathogenic for infants.

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STUDIES OF INFANT FEEDING. XI

HIGH PROTEIN FEEDING VERSUS HIGH CALCIUM ABSORPTION AS THE CAUSE OF THE INCREASE IN BODY TEMPERATURE OF INFANTS *

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INTRODUCTION

We have found the excessive calcium content of cow's milk to be a disturbing factor in many of the so-called cases of malnutrition and, as any high protein food made under ordinary conditions from cow's milk will of necessity have the greater part of the protein present as calcium caseinate, it seems to us that although protein was the apparent cause of the toxic condition resulting from the feeding to infants of a high protein milk, the real cause might be due to the calcium chemically combined in the calcium caseinate.

We have also found that the feeding to infants of large amounts of pure protein (ash-free paracasin) does not produce any unfavorable symptoms even when the protein is fed with an extremely small amount of whey.[1] As this finding may seem to be contrary to the observations of others we have continued our investigation in an endeavor to find the factor responsible for this difference.

Our investigations have shown that the reduction of the intake of inorganic salts to a point at which chlorin-free urine is eliminated resulted in a febrile condition only when large amounts of calcium was fed as calcium caseinate. We explain these observations as follows:

Under normal conditions sodium can be excreted by the kidneys as chlorid, phosphate, carbonate or sulphate while calcium can be excreted only as chlorid or acid phosphate, the phosphate being only sparingly soluble. A reduction in the intake of chlorin or phosphorus, that is to say, a reduction in the intake of whey, will not interfere with the excretion of sodium because it can form a soluble carbonate, but under the same conditions the excretion of calcium is seriously

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* Submitted for publication July 12, 1918.

* From the Boston Floating Hospital Laboratories.

* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

[1] Bosworth, A. W., and Bowditch, H. I., and Ragle, B. H.: Casein in Infant Feeding, Am. Jour. Dis. Child., 1914, **8**, 120.

interfered with and results in an accumulation or retention of calcium until a toxic condition is finally reached which results in a febrile condition accompanied by the excretion of large amounts of calcium lactate in the urine. This excretion of calcium relieves conditions temporarily, or until the calcium retained again reaches the danger point, when there will follow another fever and an increased elimination of calcium lactate. This condition is relieved by the ingestion of whey which furnishes chlorin for the elimination of the accumulated calcium as calcium chlorid.

A careful scrutiny and analysis of the conditions surrounding the data presented by Holt, Levene, and others,[2] and the data secured by us in some preliminary experiments has led us to investigate the following conditions in infant feeding:

1. The reduction of the intake of inorganic salts to a point which results in the elimination of:

(a) A chlorin-free urine.

(b) A chlorin-free and phosphorus-free urine.

(c) A chlorin-free urine accompanied by the ingestion of large amounts of sodium caseinate.

(d) A chlorin-free urine accompanied by the ingestion of large amounts of available calcium as calcium caseinate.

2. The ingestion of large amounts of calcium caseinate accompanied by the ingestion of large amounts of milk salts.

In presenting the results obtained we have selected the data from one experiment under each of the headings given above.

I. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH A CONTINUED EXCRETION OF CHLORIN-FREE URINE IS PRODUCED

The investigation began with the admission of the baby to the hospital on July 9 and may be divided into six periods as follows:

First Period, 6 p. m., July 9, to 6 p. m., July 12.—From 6 p. m., July 9, until 10 a. m., July 11 (forty hours), the child received only sterile water. From 10 a. m., July 11, to 6 p. m., July 12 (thirty-two hours), the food consisted of a mixture of 840 c.c. of whey, 420 c.c. of breast-milk and 420 c.c. of water and was divided into ten feedings. The child was on the metabolism frame during all three days.

The high output of uric acid, creatinin and creatin during the fast indicates a high endogenous metabolism and is followed by a higher excretion of these substances on the administration of food; the excretion of nitrogen, however, is lowered during the first day following the fast, indicative of a replacement of the nitrogen lost during the endogenous metabolism of the fast. During the fast the chlorin excreted was very small in amount, and both indican and acetone were detected in the urine. The child also had an acetone breath.

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[2] Holt, L. E., Levene, P. A., and others: The Influence of High Protein Feeding on the General Metabolism, Am. Jour. Dis. Child., 1912, **4**, 265.

Second Period, 6 p. m., July 12, to 6 p. m., July 22.—A period during which the food was changed several times in order to find a mixture suitable for the child. The child was not on the metabolism frame and no analytical data were secured during this period.

Third Period, 6 p. m., July 22, to 6 p. m., July 26.—The child had recovered from his intestinal trouble and was receiving the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

10 per cent. cream	160 c.c.
Buttermilk	800 c.c.
Sterile water	640 c.c.
Milk-sugar	53 gm.

Seven feedings of 210 c.c. each every twenty-four hours. Approximately 637 calories or 145 calories per kilogram body weight.

As he seemed to be in good condition and gaining in weight on this food, he was placed on the metabolism frame at 6 p. m., July 22. During this period he continued to receive the food indicated above and the urine and feces were collected and examined in order to furnish data representing his normal nitrogen metabolism. During this period the body weight increased 165 gm., an average of 41.2 gm. per twenty-four hours. He was well in every respect.

Fourth Period, 6 p. m., July 26, to 6 p. m., July 29.—The child was not on the frame during this period but received the same food given in the preceding period. No macroscopic or microscopic evidence of fat, carbohydrate or protein indigestion was found.

Fifth Period, 6 p. m., July 29, to 6 p. m., August 7.—The child was again placed on the frame and the food received was made up according to the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

10 per cent. cream	161 c.c.
Sterile water	1,439 c.c.
Lactose	89 gm.
Dry paracasein	25 gm.

Seven feedings of 210 c.c. each per twenty-four hours.

This mixture contained about the same amounts of fat, sugar and protein as the mixture given in the two preceding periods. The amount of protein ingested in twenty-four hours was less than in the case of the food made with buttermilk. This was due to the fact that it was almost impossible to manipulate the feeding-bottles so that all the paracasein was removed with the liquid portion of the food.

The inorganic salts were very much decreased in this mixture. In the preceding periods the mixtures fed contained the salts carried in the 160 c.c. of cream and the 800 c.c. of buttermilk. In the present case all the inorganic salts were derived from the 161 c.c. of 10 per cent. cream. The response to this decrease in the inorganic salt intake is shown in the lower figures obtained during this period for sodium chlorid, phosphates and acidity. The food contained 0.116 gm. of sodium chlorid per twenty-four-hour quantity while the amounts excreted dropped from 0.326 gm. the first day to nothing on the eighth and ninth days, chlorin again appearing on the tenth day (the first day of the sixth period) even with a reduction in the chlorin intake on that day. This small chlorin excretion, zero for two days even, was not accompanied by any signs of physical discomfort.

During this period the body weight increased 120 gm., an average of 13.3 gm. per twenty-four hours.

Sixth Period, 6 p. m., August 7, to 6 p. m., August 14.—From 6 p. m., August 7, and during this period the food given to the child was made according to the following formula: Fat, 2 per cent.; sugar, 6 per cent.; protein, 2 per cent.

32 per cent. cream	54 c.c.
Sterile water	1,546 c.c
Lactose	89 gm.
Dry paracasein	28 gm.

Seven feedings of 210 c.c. each per twenty-four hours.

This decreased the inorganic salts again and made the chlorin intake per twenty-four hours equal to 0.033 gm. of sodium chlorid, and the amounts excreted dropped from 0.148 gm. to 0 gm. on the fifth, sixth and seventh days. The child showed no particular discomfort as a result of this rather prolonged confinement on the metabolism frame, but on account of the loss of body weight it was thought best to discontinue the collection of urine and feces and remove the child from the frame at 6 p. m., August 14.

GENERAL DISCUSSION

In connection with the table which gives the result of our daily examination of the urines, we desire to call attention to the following points:

The acidity of the urines and the amounts of phosphates present decreased with the decrease in the amounts of whey ingested. This was to be expected as all the inorganic phosphates ingested were contained in the whey or cream used to make up the formulas. The amounts of organic phosphorus ingested were practically the same through all the periods.

The elimination of chlorin-free urine for two-day and three-day periods without symptoms of any nature is worthy of note.

A very marked increase in the ammonia output during the sixth period of the experiment is noticeable. During the fifth period the whey in the 161 c.c. of 10 per cent. cream furnished considerable neutral salts of organic acids (citrates, albuminates, etc.), the bases of which could be used to neutralize the acid bodies eliminated in the urine. During the sixth period, however, the intake of such base-carrying substances was much reduced, and sufficient bases were not ingested to neutralize the acid bodies eliminated in the urine. This resulted in an immediate increase in the amount of ammonia in the urine with a corresponding decrease in the urea. For the twenty-four hours ending at 6 p. m., August 7, the urine contained 0.261 gm. of nitrogen present as ammonia, and for the twenty-four-hour period ending at 6 p. m., August 8, the first day of the reduction of the intake of the salts to the lowest figure, the urine contained 0.522 gm. of nitrogen in the form of ammonia, an increase of 100 per cent. in one day.

It will be noticed that only a small part of the ammonia is necessary to neutralize the phosphates. Just what the nature of the acid bodies is we are not able to state. We did not detect the presence of acetone bodies in the urine at any time during this period.

TABLE 1.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS

Date*	Body Weight, Gm.	Urine											Average N. in Feces, Gm.
		Volume, C.c.	Specific Gravity	Total Acid, N/10, C.c.	P_2O_5, Gm.	Cl as NaCl, Gm.	Total N, Gm.	N as NH_3, Gm.	N as Urea, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	
7/10†‡	4,500	505	1.007	82.8	0.577	0.024	1.513	0.161	1.111	0.107	0.030	0.041	....
1/11†‡	....	630	1.005	54.2	0.534	0.048	1.658	0.247	1.064	0.131	0.028	0.068	....
7/12†	4,540	670	1.005	144.7	0.574	0.206	1.294	0.110	0.884	0.243	0.037	0.065	.....
7/12-22													
7/23	4,480	700	1.006	127.4	0.810	0.913	1.372	0.319	0.896	0.065	0.020	0.026	0.365
7/24	...	660	1.006	97.7	0.918	0.800	1.774	0.292	1.279	0.057	0.019	0.024	0.365
7/25	....	980	1.006	156.8	1.129	1.180	2.387	0.274	1.949	0.084	0.021	0.030	0.365
7/26	4,645	990	1.007	134.6	1.161	1.709	2.550	0.360	2.051	0.084	0.021	0.034	0.365
7/26-29													
7/30	4,730	1,200	1.004	98.4	0.760	0.326	1.747	0.175	....	0.053	0.022	0.020	0.173
7/31	....	1,220	1.003	41.5	0.386	0.332	1.264	0.164	0.929	0.078	0.022	0.030	0.173
8/1	....	1,300	1.002	41.6	0.398	0.110	1.092	0.175	0.845	0.053	0.023	0.020	0.173
8/2	....	1,240	1.002	39.7	0.379	0.298	1.146	0.208	0.724	0.066	0.021	0.025	0.173
8/3	....	1,070	1.003	42.8	0.317	0.223	1.079	0.216	0.713	0.057	0.019	0.022	.....
8/4	....	670	1.003	24.1	0.233	0.115	0.975	0.173	0.522	0.045	0.018	0.021	..
8/5	....	1,170	1.003	56.2	0.370	0.047	1.409	0.216	0.963	0.081	0.020	0.028	..
8/6	....	1,060	1.003	33.9	0.357	0.000	1.676	0.261	....	0.072	0.020	0.029	.
8/7	4,850	1,060	1.003	33.9	0.357	0.000	1.676	0.261	....	0.072	0.020	0.029	.
8/8	....	1,000	1.002	38.2	0.232	0.148	1.039	0.522	0.284	0.072	0.020	0.017	....
8/9	..	850	1.003	47.6	0.390	0.065	1.275	0.509	....	0.084	0.020	0.015	.....
8/10	..	970	1.003	26.6	0.317	0.067	1.249	0.494	....	0.082	0.022	0.019	.
8/11	...	1,060	1.003	27.6	0.378	0.015	1.276	0.392	0.613	0.086	0.020	0.020	.....
8/12	....	1,000	1.003	32.0	0.275	0.000	1.036	0.476	....	0.087	0.017	0.015	.
8/13	....	900	1.005	28.8	0.303	0.000	1.411	0.731	....	0.075	0.017	0.019	...
8/14	4,510	760	1.003	33.4	0.357	0.000	1.105	0.655	0.378	0.092	0.020	0.017	.....

* Twenty-four-hour period ending 6 p. m. † Traces of indican appeared in the urine on these days. ‡ Traces of acetone on these days.

The amounts of creatinin and creatin excreted during the fasting period were much above the normal as would be expected. During the other three periods the creatinin figures are strikingly uniform.

During the third period, when the food contained an excess of all constituents, the child increased in body weight an average of 41.2 gm. per twenty-four hours and the creatin output averaged 0.028 gm. per day. In the fifth period when the whey had been reduced to the amount carried in 161 c.c. of 10 per cent. cream, the average daily increase in body weight was reduced to 13.3 gm. and the average daily creatin excretion was 0.025 gm. In the sixth period there was an average daily decrease in body weight of 48.6 gm., and the average daily excretion of creatin was 0.015 gm. with a daily fluctuation giving figures between 0.027 and 0.015 gm.

No symptoms of any nature developed during the fifth and sixth periods.

II. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH A CONTINUOUS EXCRETION OF CHLORIN-FREE AND PHOSPHORUS-FREE URINE IS PRODUCED

We have shown in a previous paper how the feeding of an excessive amount of calcium may result in the precipitation within the intestines of all the ingested phosphorus as insoluble calcium phosphate and thus reduce the phosphorus metabolism to such a low level that the urine becomes phosphorus-free and contains a large amount of carbon dioxid.[3]

We have been able to take advantage of this fact and, by the feeding of a synthetic food containing no inorganic salts but considerable soluble calcium, we have reduced the chlorin intake and output to nil and brought about the excretion of a phosphorus-free urine.

This investigation began when the child was placed on the metabolism frame, July 13, 1915, and may be divided into two periods.

First Period, 9 a. m., July 13, to 9 a. m., July 14.—During this first twenty-four hours the child received 1,260 c.c. of a modified milk containing 2 per cent. of fat, 6 per cent. of lactose and 2 per cent. of protein.

Second Period, 9 a. m., July 14, to 9 a. m., July 22.—During the next eight days the child received a chlorin-free synthetic[4] milk containing pure butter fat, 2 per cent.; lactose, 6 per cent.; sodium caseinate, 2 per cent., and calcium acetate [$(CH_3COO)_2Ca.H_2O$)] 0.167 per cent. The only phosphorus present in this food was that contained within the casein molecule. The child received 1,260 c.c. of this food every twenty-four hours.

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[3] Bowditch, H. I., and Bosworth, A. W.: Boston Med. and Surg. Jour., 1917, **177**, 864.

[4] Bowditch, H. I., and Bosworth, A. W.: Studies of Infant Feeding, Tr. Am. Ped. Soc., 1916, **28**, 114.

The data secured will be found in Table 2. By consulting the table it will be noticed that the urine became alkaline on the first day of the second period and remained so while the child received the synthetic milk. All the urines during this period were heavily charged with carbon dioxid, the addition of a drop of hydrochloric acid causing a marked effervescence.

The urine became chlorin-free on the first day of the second period and phosphorus-free on the fourth day. A marked increase in the ammonia excretion is noticed during the time the child received the food containing no milk salts. Most of the phosphoric acid resulting from the digestion of the casein was precipitated in the intestines as insoluble calcium phosphate and appeared as such in the feces. The remainder must have been assimilated and retained, for the urine soon became phosphorus-free.

No symptoms of any kind developed during this experiment.

III. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT WHERE A CONTINUED EXCRETION OF CHLORIN-FREE URINE IS PRODUCED ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF SODIUM CASEINATE

The child selected for this experiment was 11 months old, weighed 7,129 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 9:30 a. m., July 26. The investigation may be divided into two periods.

First Period, July 26, to July 27.—During the first twenty-four hours the child received a food made up as follows:

Whole milk	75 c.c.
Dextri-maltose to make total sugar	5%
Boiled water to make	100 c.c.

Five feedings, 227 c.c. each.

This food contained fat, 3 per cent.; sugar, 5 per cent., and protein 2.4 per cent.

Second Period, July 27 to August 7.—At 9:30 a. m., July 27, the food was changed to a synthetic milk containing fat, 2 per cent.; sugar, 6 per cent., and sodium caseinate, 6.5 per cent. He received five feedings of 227 c.c. each per day. The feces was so small in amount that no work was done on it. (In this connection see a previous paper by us.[5])

The data secured will be found in Table 3. Here we again have an alkaline urine containing large amounts of carbonate and ammonia. The uric acid, creatinin and creatin outputs show no marked variations from day to day. No symptoms of any nature developed.

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[5] Bowditch, H. I., and Bosworth, A. W.: Boston Med. and Surg. Jour., 1917, **177,** 864.

TABLE 2.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS TO A POINT WHICH RESULTS IN THE EXCRETION OF A CHLORIN- AND PHOSPHORUS-FREE URINE

24-Hour Period Ending 1915	Body Weight, Gm.	Urine									Feces			
		Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	P_2O_5, Gm.	Chlorin, Gm.	Total N Gm.	N as NH_3 Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.	Dry Weight, Gm.	Fat, Gm.	Calcium Oxid, Gm.	Phosphoric Oxid, Gm.
8/14	5,336	510	1.009	113.2	0.816	0.707	1.948	0.251	0.057	None	12.15	5.01	0.937	0.363
8/15	....	260	1.014	Alk.	0.286	None	1.877	0.497	0.058	None	7.67	3.03	0.571	0.186
8/16	....	530	1.008	Alk.	0.133	None	1.677	0.502	0.062	None	7.06	1.88	0.660	0.131
8/17	...	410	1.009	Alk.	0.082	None	1.484	0.786	0.048	None	7.47	3.07	0.573	0.126
8/18	....	300	1.012	Alk.	0.054	None	1.490	0.572	0.045	None	9.28	3.04	0.904	0.213
8/19	....	300	1.011	Alk.	None	None	1.374	0.539	0.030	None	3.58	0.87	0.243	0.084
8/20	....	240	1.010	Alk.	None	None	1.291	0.304	0.040	None	6.68	2.55	0.565	0.175
8/21	....	480	1.007	Alk.	None	None	1.032	0.454	0.046	None	6.50	2.41	0.612	0.150
8/22	4,768	420	1.006	Alk.	None	None	0.997	0.316	0.041	None	5.27	2.46	0.457	0.128

TABLE 3.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS AND FEEDING LARGE AMOUNTS OF SODIUM CASEINATE

24-Hour Period Ending	Body Weight, Gm.	Urine											
		Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	Phosphori Oxid, Gm.	Total N, Gm.	N as NH Gm.	Uric Acid, Gm.	Creatinin, Gm	Creatin, Gm	Calcium Oxid, Gm.	Lactic Acid, Gm.
7/27	7,129	640	1.008	83.2	0.672	0.826	2.87	0.39	0.147	0.078	0.089	0.029	None
7/28	..	760	1.010	Alk.	0.349	0.456	4.36	0.85	0.120	0.074	0.075	0.056	None
7/29	....	780	1.011	Alk.	0.137	0.741	5.13	2.88	0.110	0.078	0.020	0.055	None
7/30	..	830	1.011	Alk.	0.145	0.315	6.51	0.49	0.089	0.072	0.050	0.076	None
7/31	....	810	1.011	Alk.	0.062	0.194	5.90	0.41	0.092	0.071	0.050	0.060	None
8/1	...	840	1.013	Alk.	0.017	0.378	6.88	0.85	0.120	0.080	0.065	0.077	None
8/2	...	840	1.010	Alk.	0.082	0.294	8.47	0.85	0.073	0.074	0.074	0.097	None
8/3	....	1,020	1.010	Alk.	0.092	0.306	7.14	1.26	0.119	0.077	0.072	0.135	None
8/4	....	840	1.010	Alk.	0.000	0.377	8.88	2.42	0.092	0.069	0.060	0.068	None
8/5	....	760	1.013	Alk.	0.000	0.800	7.02	3.02	0.076	0.066	0.048	0.041	None
8/6	....	570	1.013	Alk.	0.000	0.500	8.06	3.17	0.084	0.072	0.050	0.031	None
8/7	7,013	680	1.011	Alk.	0.000	0.200	8.85	2.53	0.107	0.081	0.070	0.064	None

IV. THE REDUCTION OF THE INTAKE OF INORGANIC SALTS TO A POINT AT WHICH CHLORIN-FREE URINE IS EXCRETED, ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF CALCIUM CASEINATE

The child selected was 10 months old, weighed 5,477 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 8 p. m., July 11. The investigation may be divided into two periods.

First Period, July 11 to July 12.—During the first twenty-four hours the child received a food made up as follows:

Fat-free milk	75 c.c.
Dextri-maltose	5 gm.
Boiled water to make	100 c.c.

Six feedings, 170 c.c. each.

This food contained fat, a trace; sugar, 8 per cent., and protein 2.4 per cent.

Second Period, July 12 to July 18.—At 8 p. m., July 12, the food was changed to one made according to the following formula:

32 per cent. cream	65 c.c.
20 per cent. lactose solution	377 c.c.
Calcium caseinate	87 gm.
Sodium citrate	80 grains
Water to make	1,392 c.c.

Six feedings, 170 c.c. each.

This food contained fat, 1.50 per cent.; sugar, 5.63 per cent.; protein, 6.25 per cent., and calcium oxid, 0.1575 per cent. The data secured during this experiment will be found in Table 4 and Chart 1. The food used for this investigation had a low chlorin and high calcium content.

The most striking point brought out by the data in Table 4 is the appearance of lactic acid in the urine on the 15th, followed by a toxic condition which manifested itself during the night of the 16th. The appearance of the lactic acid is accompanied by a greatly increased elimination of calcium. It will be noticed that the temperature of 102.4 F. recorded on the morning of the 17th is reduced during the day and seemed to be directly associated with the ingestion of the early morning feeding. Possibly the lactose in the food had some influence in reducing the temperature.

The lactic acid was determined by extracting the acidulated urine with ether, distilling off the ether, dissolving the residue in water, evaporating to a thick syrup, taking up with water, converting the lactic acid to the zinc salt by the addition of zinc oxid, boiling, filtering, evaporating the filtrate to dryness, drying in the oven for two hours and weighing. The weights were checked by burning the zinc lactate and weighing the residual zinc oxid. The lactic acid was identified by the crystals of zinc lactate.

Owing to the uncomfortable condition of the child, he was removed from the metabolism frame on the 18th, but continued to receive the

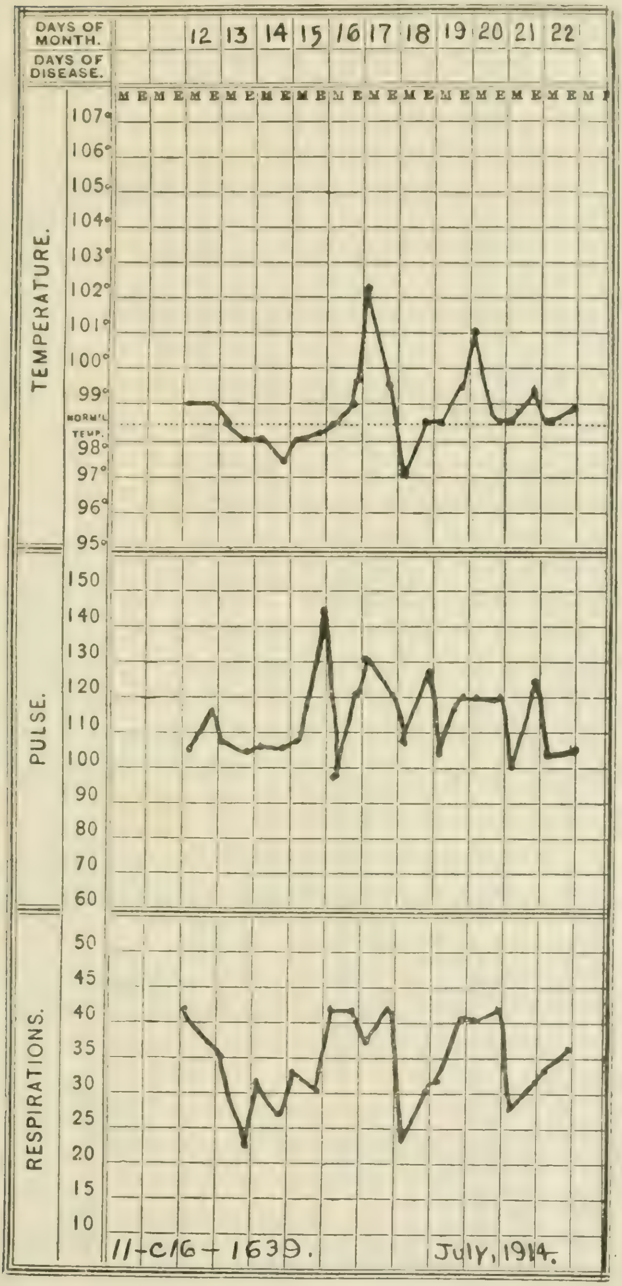

Chart 1. Record of the temperature, pulse and respiration as observed in connection with the tests outlined in Table 4.

same food until the morning of the 21st. During the night of the 19th another temperature was noticed which also seemed to be lowered by the ingestion of food.

The greatly increased elimination of uric acid, creatinin and creatin during this experiment is to be expected as a result of the fever. It is worthy of note that none of the urines in this set showed the presence of carbonates.

The toxic condition produced during this experiment we believe to be due to the following circumstances. The digestion of fat and protein within the intestine results in the production of acids, fatty acids from fat and amino-acids or polypeptic acids from the proteins. These acids do not remain as free acids but immediately unite with the bases present in the intestines to form salts, the soluble salts being absorbed, the insoluble salts being eliminated in the feces. In the presence of the large amount of calcium carried into the intestines in combination with the casein many more of these acids form calcium salts than would be the condition under more normal circumstances. The soluble organic salts are carried to the tissues and the organic part used for vital activities leaving as refuse the base calcium which has acted simply as a conveyor and neutralizer. Under normal conditions this calcium would form chlorid or phosphate and be eliminated in the urine immediately. Under the conditions of this experiment there was no chlorin available for such purpose and very little phosphorus. The result is an accumulation of calcium until a toxic condition is reached and then, during the fever, an abundant elimination of soluble calcium lactate.

V. THE FEEDING OF LARGE AMOUNTS OF CALCIUM CASEINATE WHEN ACCOMPANIED BY THE INGESTION OF LARGE AMOUNTS OF INORGANIC SALTS (WHEY)

The child selected was 5 months old, weighed 5,371 gm., and seemed to be in good physical condition. He was placed on the metabolism frame at 8 p. m., July 11. The investigation may be divided into two periods.

First Period, July 11 to July 12.—During the first twenty-four hours the child received a food made up as follows:

Whole milk	60 c.c.
Boiled water	40 c.c.
Maltose to make sugar	6%

Six feedings, 170 c.c. each.

This food contained, fat, 2.4 per cent.; sugar, 6 per cent., and protein 1.9 per cent.

TABLE 4.—Showing Change in Composition of Urine as a Result of Reducing the Intake of Inorganic Salts and Feeding Large Amounts of Calcium Caseinate

24-Hour Period Ending at 8 p. m., 1914	Urine												Feces			
	Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm.	P₂O₅, Gm.	Total Nitrogen, Gm.	Nitrogen, as Ammonia, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm.	Dry Weight, Gm.	Total N, Gm.	P₂O₅, Gm.	Calcium Oxid, Gm.
7/12	660	1.010	59.4	0.809	0.53	3.53	0.340	0.145	0.086	0.034	0.0462	0.0000	10.1	0.606	0.170	1.075
7/13	720	1.009	13.0	0.655	0.36	4.29	0.363	0.092	0.060	0.049	0.0432	0.0000	9.1	0.528	0.122	0.901
7/14	750	1.010	123.0*	0.394	0.34	4.83	0.522	0.085	0.072	0.023	0.0875	0.0000	9.0	0.653	0.109	0.603
7/15	626	1.011	89.2*	0.031	0.95	4.62	1.403	0.186	0.097	0.052	0.1640	0.2799	13.0	0.868	0.222	0.902
7/16	680	1.013	21.8*	0.000	0.20	5.21	0.823	0.336	0.113	0.127	0.1537	0.5208	14.0	0.963	0.252	1.244
7/17	650	1.016	27.3	0.073	0.31	6.64	0.454	0.325	0.100	0.100	0.1274	0.3608	14.5	0.931	0.246	0.940
7/18	730	1.015	2.9	0.000	0.22	6.95	1.083	0.380	0.123	0.083	0.2015	0.4075	....	....	....	....

* Alkalinity.

TABLE 5.—Showing Composition of the Urine when Large Amounts of Calcium Caseinate Is Ingested Accompanied by Large Amounts of Inorganic Salts (Whey)

24 Hour Period Ending at 8 p. m., 1914	Volume, C.c.	Specific Gravity	Total Acidity as C.c. of N/10	Chlorin, Gm	P₂O₅, Gm.	Total Nitrogen, Gm.	Nitrogen as Ammonia, Gm.	Uric Acid, Gm.	Creatinin, Gm.	Creatin, Gm.	Calcium Oxid, Gm.	Lactic Acid, Gm
7/12	600	1.010	30.0	0.714	0.68	2.50	0.285	0.107	0.071	0.042	0.0132	0
7/13	620	1.010	20.0*	0.408	0.59	2.97	0.576	0.099	0.071	0.045	0.0372	0
7/14	580	1.013	93.0*	0.304	0.33	4.93	0.601	0.085	0.070	0.054	0.0172	0
7/15	670	1.014	60.0*	0.304	0.37	5.07	0.657	0.107	0.070	0.065	0.0558	0
7/16	740	1.013	59.0*	0.622	0.31	8.88	0.315	0.096	0.072	0.073	0.1154	0
7/17	670	1.014	36.0*	0.539	0.35	8.85	0.555	0.103	0.074	0.052	0.1072	0
7/18	730	1.015	48.0*	1.613	0.45	8.47	0.220	0.100	0.073	0.050	0.0847	0

* Alkalinity.

Second Period, July 12 to July 18.—At 8 p. m., July 12, the food was changed to one made according to the following formula:

32 per cent. cream	65 c.c.
20 per cent. lactose solution	331 c.c.
Calcium caseinate	87 gm.
Sodium citrate	80 grains
Whey	580 c.c.
Water to make	1,392 c.c.

Six feedings, 170 c.c. each.

This food contained, fat, 1.50 per cent.; sugar, 6.4 per cent., and calcium oxid, 0.1575 per cent.

The data secured will be found in Table 5. In this case sufficient chlorin and phosphorus had been ingested to permit the elimination of all the calcium as soluble chlorid or phosphate, and our data shows nothing worthy of note, the ingestion of the large amount of calcium causing no upset in the condition of the child.

CONCLUSIONS

We have shown that the ingestion of large amounts of calcium and the absorption of this calcium as organic salts, if not accompanied by the ingestion of sufficient chlorin or phosphorus to permit of the formation of soluble salts will result in an accumulation of calcium in the tissues which is followed by a toxic condition and the elimination of calcium lactate in the urine.

The toxic condition noticed by others when a high protein synthetic food was fed was probably the result of the high calcium content of the food, as our work reported in this and previous papers seems to indicate, and not the result of the high protein content, the protein being responsible only to the extent that it is the carrier of the calcium in the form of calcium caseinate.

Whether the toxic condition noticed is the result of the accumulated calcium itself or to a calcium salt, possibly calcium oxalate, we are not prepared to state.

C. Bruger[6] has recorded the fact that the injection of neutral or alkaline phosphates of sodium resulted in a diminution in the calcium content of the serum and a condition of tetany. In view of the fact that the overloading of the serum with neutral or alkaline phosphates would favor the precipitation of calcium salts we are inclined to believe our results and his to be manifestations of the same phenomenon.

We also believe the observations of Marriott and Howland,[7] in which they noticed a diminution in the calcium content of the serum and a marked phosphorus retention, to have some bearing on the same phenomenon.

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[6] Bruger, C.: Toxicity of Phosphates in Relation to Blood Calcium and Tetany, Jour. Pharmacol., 1917, **10**, 105.

[7] Marriott, W. McK., and Howland, John: Phosphate Retention as a Factor in the Production of Acidosis in Nephritis, Arch. Int. Med., 1916, **18**, 108.

THE EFFECT OF ALKALI AND MALT PREPARATIONS ON THE RETENTION OF CALCIUM IN INFANCY *

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There is no paucity of literature concerning the metabolism of calcium in infancy, but very little is known regarding the factors that may influence it; even the effect of the organic ingredients of milk, with the exception of fat, has been very little studied, and there are many facts regarding the influence of fat that are not entirely clear. There is a still greater gap in our knowledge with regard to the effect of inorganic compounds on calcium metabolism. How calcium salts themselves act on the retention of calcium has been studied to a certain extent, it is true, but as to the influence of other salts, our knowledge remains very meager.

THE EFFECTS OF ALKALI

Dugois and Stolte[1] were the first to study the effect of alkali on calcium retention in infancy. They attribute the favorable effect of Keller's malt soup on calcium retention to the alkali contained in it. In an endeavor to prove this they made observations on two children in six periods. They believed that they showed a favorable influence of the alkali on calcium retention. Their results, however, were so very irregular, that it is hard to accept them as conclusive. For instance, in one experiment there was a very distinct loss of calcium in the control period and only a slight retention in the period with alkali. The difference in the calcium balance between the two periods was very great but was due not so much to satisfactory retention in the alkali period as to a very marked loss in the control period. The other two experiments were not very impressive, the difference being very slight in the amount of calcium retained. To explain their peculiar results they maintain that "the smaller the balance of calcium was at first, the greater became the increase of calcium retention." The explanation that they offer that every increase of alkali contributes to neutralize the acids produced in metabolism, thus saving the body calcium, does not seem very likely. Calcium plays a very small part in the neutralization of the ordinary acids of metabolism and ammonia would be much more readily available than would calcium.

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* Submitted for publication July 10, 1918.

* From the Harriet Lane Home and from the Department of Pediatrics, Johns Hopkins University.

[1] Dubois, M., and Stolte, K.: Jahrb. f. Kinderh., 1913, **77,** 21.

In the case of adults, Rumpf[2] found an increase of calcium excretion of 50 per cent. when sodium lactate and lactic acid were given, while Lunin demonstrated that sodium carbonate would diminish the excretion of calcium in the stool. Rumpf found the same with sodium phosphate and sodium sulphate.

Recently Givens and Mendel[3] have made animal experiments in which they not only failed to find any favorable effects of alkali, but, on the contrary, obtained a rather unfavorable effect on calcium retention, though they concluded reservedly that the administration of base produced no significant effect on the calcium balance in the dog. There is the possibility that if young animals had been used, the results might have been different, but this is only a conjecture.

AUTHOR'S EXPERIMENTS

I wished to determine on the same child and with the same malt preparation whether the beneficial effect on the calcium retention attributed to malt extracts is due to the extract itself or to the added alkali. For this reason I used a liquid malt preparation (maltine plain) which contained by analysis from 50 to 54 per cent. maltose and from 1.3 to 1.5 per cent. dextrine, expressed as glucose, containing no additional alkali. During certain periods alkali in the form of sodium bicarbonate was added.

The child used for the observations was a vigorous but not very well nourished infant of fourteen months. There was no recognizable disease and no evidence of rickets. Except for a mild attack of bronchitis, at which time the experiment was interrupted, he remained well throughout the whole period of observation.

Experimental periods for calcium metabolism should be as long as possible. The duration of each period was four days. Short periods are unsatisfactory for the study of calcium metabolism. The stools contain a large amount of calcium. The longer the period, the less the influence of incomplete stool collection. At the beginning of each fore-period, the diet for each entire period was made up at one time, sterilized and preserved on ice. The analysis of the food was made in triplicate. The interval between the periods was at least three days. The infant was put on the special diet for each period for two days before the collection of specimens was begun. The infant was on a special metabolism bed. The collection of urine and feces was completely satisfactory throughout the experiment.

Calcium was determined by McCrudden's method, nitrogen by the method of Folin and Farmer, fat by the Babcock apparatus and

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[2] Cited by O. Rommel., Arch. f. Kinderh., 1903, **37,** 261.

[3] Givens and Mendel: Jour. Biol. Chem., 1917, **31,** 427.

TABLE 1.—RESULTS OF EXPERIMENTS TO DETERMINE THE CALCIUM RETENTION IN A 14 MONTHS' OLD CHILD

Period	Food (per Diem)						Stools		Body Weight		Calcium (as CaO) per Diem		
	Whole Milk				Alkali* ($NaHCO_3$)	Maltine Plain	Number During Period	Consistency	Before and After the Period, Gm.	Difference, Gm.	Intake	Output	Retention
	Protein, %	Fat, %	Sugar, %	Amount								Urine Stool	
I	2.2	2.6	5.0	213 c.c. ×5	....	....	7	Mostly formed	8,060 7,900	- 100	2.151	0.054 1.932 1,986	- 0.165
II	2.5	3.5	4.8	213 c.c. ×5	4% solution (10 c.c. × 5) = 2 gm. per day	.. ..	8	Mostly formed	7,630 7,660	+ 30	1.891	0.037 1.693 1.730	+ 0.161
III	2.3	2.8	5.0	213 c.c. ×5	....	....	11	Formed	7,660 7,760	+ 100	2.049	0.046 1.715 1.761	+ 0.288
IV	2.2	2.8	4.9	213 c.c. ×5	6% solution (10 c.c. × 5) = 3 gm. per day	....	12	2 hard 2 soft 8 formed	8,035 8,005	- 30	1.968	0.019 1.874 1.893	+ 0.075
V	2.5	2.8	5.2	213 c.c. ×5	....	11 c.c. × 5	6	All pasty	8,300 8,310	+ 10	2.124	0.041 1.476 1.517	+ 0.607
VI	2.4	3.2	5.0	213 c.c. ×5	6% solution (10 c.c. × 5) = 3 gm. per day	11 c.c. × 5	12	Mostly formed	8,500 8,515	+ 15	2.115	0.024 2.276 2.302	- 0.187
VII	2.1	2.6	6.4	213 c.c. ×5	....	....	10	Formed	8,250 8,150	—100	1.994	0.032 1.683 1.715	+ 0.279
VIII	2.5	2.8	4.7	213 c.c. ×5	....	11 c.c. × 5	13	Formed	8,175 8,270	+ 95	2.201	0.030 1.842 1.872	+ 0.329

* Alkali solutions were kept separately and mixed with the food just before feeding.

carbohydrate by Shimidzu's[4] method. The analytic results are given in Table 1. They are calculated on a twenty-four hour basis.

Table 1 shows that there was some variation in the amount of the organic ingredients as well as calcium in the specimens of milk. The differences, however, were not great enough to have any possible effect on the retention of calcium, whereas the bicarbonate and maltine added were in amounts large enough to be considered as new factors.

DISCUSSION OF THE RESULTS

If the average results of similar periods are investigated, they will be found to be as summarized in Table 2.

TABLE 2.—Summary of the Average Results of Similar Periods

Additions to Whole Milk	Number of Period	Retention of Calcium (CaO)	
		Absolute, Gm.	Average, Gm.
0	I	+0.165	+0.244
0	III	+0.288	
0	VII	+0.279	
Alkali 2 gm. $NaHCO_3$	II	+0.161	+0.118
3 gm. $NaHCO_3$	IV	+0.075	
Maltine plain	V	+0.607	+0.468
Maltine plain	VIII	+0.329	
Maltine plain and alkali	VI	—0.187	

It is very clear at first sight that the retention of calcium in the average whole milk period is twice as large as that in the average alkali period. The retention was not so bad in Period II, in which alkali was used, especially if it is compared with Period I, but the retention of Period I is the worst in all the three "plain" periods, whereas the amount of alkali used in Period II was smaller than in the other alkali periods. The impression that one receives is that calcium retention becomes worse as the alkali added increases in amount. It is therefore possible to say that it is not through the alkali itself that malt extract acts favorably on calcium storage. The quantity of alkali, in proportion to the amount of whole milk given, that was used by Dubois, Stolte and by myself was approximately the same. They used the equivalent of 34 c.c. of normal alkali per liter of whole milk whilst I used the equivalent of from 24 to 36 c.c. of normal alkali per liter of whole milk. It is necessary to make the basis of comparison on the amount of milk taken as Dubois and Stolte do not give the weight of the two children used for their observations.

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[4] Shimidzu: Biochem. Ztschr., 1908, **13,** 243.

What, then, if malt extract is used with alkali, as the usual preparation of malt extract contains some alkali? Period VI gives the answer. This is the period in which the calcium balance was negative. Though this experiment with malt extract and alkali was not repeated, yet the results, taken with those of other periods, are conclusive enough to show that there is no favorable effect from the alkali, even when this is combined with a malt preparation.

On the other hand, in the periods in which the malt extract alone was administered, the result was quite definite. The average retention during the two maltine periods was almost twice as great as that during the whole milk periods. The balance was especially good in Period V, in which the infant had only six stools, which were all loose and pasty. In Periods VI and VIII the stools were not noticeably different in number and consistency from those in the other periods, with the exception of Period V. It is thus evident that it is the malt preparation and not the alkali which affects calcium storage favorably. It is true that the usual malt extract preparations used in infant feeding contain alkali but this is usually too small in amount to act as an unfavorable factor. In these experiments may be seen the effects of malt extract alone.

EFFECT OF CARBOHYDRATE ON CALCIUM RETENTION

Strictly speaking there is not a single report of the effect of carbohydrate on calcium which is quite free of criticism. Rothberg[5] and Birk[6] determined the effect of the organic ingredients of milk on the calcium balance. This work, however, was not well planned to demonstrate any effect from the carbohydrates alone because when the fat of the food was increased it was not done without at the same time changing the carbohydrate content of the food. One cannot draw from their experiments any definite conclusions regarding carbohydrates in general, or of malt preparations in particular, nor can we derive any definite information regarding the effect of malt preparations from the work of Arndt[7] or Freund.[8] In an attempt to follow the fate of fat in the intestines of infancy, Usuki[9] found a favorable effect from Keller's malt soup extract on calcium retention. Each infant retained much more calcium when malt extract was used than when simple maltose was used. The question is: To what does malt extract owe this favorable influence, carbohydrate or alkali?

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[5] Rothberg: Jahrb. f. Kinderh., 1907, **66,** 69.

[6] Birk: Jahrb. f. Kinderh., 1907, **66,** 300.

[7] Arndt: Inaug. Diss. Breslau, 1901, cited by Rothberg, Jahrb. f. Kinderh., 1907, **66,** 71.

[8] Freund: Biochem. Ztschr., 1907, **16,** 471.

[9] Usuki: Jahrb. f. Kinderh., 1910, **72,** 42.

Preparations which come under the name of malt extract contain a number of different substances unknown as well as known. It was shown by Usuki that it is not maltose alone which exerts the favorable effect. Our knowledge is still too poor to be able to judge of the effect of a simple carbohydrate, even of lactose itself. There is not sufficient nitrogenous matter in the extract to ever exercise an appreciable influence in either direction. The total nitrogen of our malt extracts was 1.2 and 0.98 gm. in 100 c.c. of the specimens used in Period V and Periods VI and VIII, respectively. There is a small amount of ash in malt extract but in the amounts used in the milk dilutions this is hardly great enough to exert any influence. Thus, one of the chief constituents is phosphoric oxid. My analysis showed that the specimens used in Period V and Periods VI and VIII contained 0.305 and 0.311 gm. of phosphoric oxid in 100 c.c., respectively, or 0.153 and 0.156 gm. in twenty-four hours. This amount is of no consequence when it is considered that milk contains about 0.7 gm. phosphoric oxid in 100 c.c. and from the milk the infant received 7.45 gm. of phosphoric oxid each day.

We cannot discover the substance or substances which alone affect calcium retention favorably, but we can say safely of malt extract that it is not the alkali in it or the alkali added to it which acts beneficially on calcium storage. It is rather the malt extract itself—the malt extract without alkali.

CONCLUSIONS

In a normal infant the addition of alkali to milk produced not only no favorable effect on the retention of calcium but a distinctly unfavorable one.

Malt extract alone without alkali acts beneficially on calcium storage.

If malt soup has a favorable effect on calcium metabolism, it is not as a result of the alkali originally contained in it or added to it.

Malt extract to which a considerable amount of alkali has been added seems to have a rather unfavorable influence on the calcium balance.

THE RELATIVE EFFICIENCY OF THE DIFFERENT MERCURIAL PREPARATIONS IN THE TREATMENT OF CONGENITAL SYPHILIS IN INFANTS AND CHILDREN

AS DETERMINED BY A QUANTITATIVE ANALYSIS OF THE MERCURY ELIMINATED IN THE URINE *

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In spite of the different forms of arsenic used under various trade names, mercury, in some form, still holds the foremost place in the treatment of syphilis. Even when the arsenic preparations are used, mercury is usually continued for long periods in order to effect a cure.

Many of the salts of mercury, including metallic mercury itself, are administered in various ways: by mouth, by insufflation, subcutaneously and by inunction.

ABSORPTION AND ELIMINATION OF MERCURY

Owing to the difficulty in detecting mercury in the body fluids, little light has been thrown on the question as to what extent the different forms of mercury were absorbed and how eliminated. Meyer and Gottleib[1] state, "the excretion of mercury in the urine offers a means of estimating the amounts of mercury circulating in the body and the duration of its action. After absorption it circulates as a compound of mercury albuminate and sodium chlorid. It is chiefly excreted in the feces and only small amounts in the urine, and that the mercury present in the circulation probably maintains a definite ratio to the amount excreted in the urine." "The determination of the curves of elimination of mercury is of importance for the estimation of the value of different methods of administration." [2] Jones[3] states, "mer-

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* Submitted for publication July 15, 1918.

* Read at the meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

[1] Meyer and Gottleib: Pharmacology, Clinical and Experimental. Philadelphia, J. B. Lippincott Company.

[2] Burgi: Arch. f. Dermatol. u. Syph., **79,** 1906.

[3] Jones: Brit. Med. Jour., 1888, p. 660.

cury is chiefly eliminated by the urine and when it causes purgation, more is eliminated by the bowel."

Whether mercury by inunction is absorbed by the skin, has long been a cource of controversy. Up to the present year, many of the foremost authorities have claimed that no mercury was absorbed by the skin, but that the mercury was volatilized by means of the body heat and absorbed through the respiratory tract.

Wile and Elliot,[4] by employing a modification of the Reinsch method, were able to detect as small an amount of mercury as 0.025 mg. in 300 c.c. of urine. By using this method they were able to demonstrate that "the mode of absorption of mercury in the inunction cure is both by volatilization and by direct absorption through the skin." Schamberg, Kolmer, Raiziss and Gavron,[5] in an experimental study on rabbits, were able to demonstrate that "the chief avenue of absorption of mercury when applied by inunction is the skin and that rabbits may be fatally poisoned with mercury by inunction, even when no opportunity of absorption through the lungs exists."

LITERATURE ON THIS SUBJECT

So far as we have been able to determine in reviewing the literature, no work has been done on the elimination of mercury in the treatment of syphilis in infants and children.

Up to the present time, the form, dose and method of administration of mercury in the treatment of syphilis in infants and children have been more or less haphazard. Almost all of the modes are in vogue, the physician using the method which seems in his hands, to produce the best clinical results or, frequently, the one which may be given with the least suspicion as to what is being given.

Whatever form of mercury is administered, the object has been to produce a disappearance of the symptoms of syphilis and maintain the mercurial dosage in such quantities, for long periods of time, as to keep within the tolerance as indicated by salivation and diarrhea. That mercury, even by inunction in sufficient doses, is toxic to rabbits was shown in the experiments by Schamberg and his associates.[5] In these experiments five rabbits were given from two to four inunctions of calomel ointment or mercury ointment. All of the rabbits died and showed acute hyperemia of the glomeruli and cloudy swelling of the parenchyma.

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[4] Wile and Elliot: Mode of Absorption of Mercury in the Inunction Treatment of Syphilis, Jour. Am. Med. Assn., 1917, **68,** 1024; Jour. Cutan. Dis., 1917, **35,** 594.

[5] Schamberg, Kolmer, Raiziss and Gavron: Experimental Studies of the Mode of Absorption of Mercury When Applied by Inunction, Jour. Am. Med. Assn., 1918, **70,** 142.

OBJECT OF THE AUTHORS' EXPERIMENTS

Our series of experiments was undertaken to determine, if possible, the extent of absorption of mercury into the circulation as indicated by the elimination in the urine, when the ordinary methods and dosage were employed and the time during which mercury continues to be eliminated in the urine after the mercury has been discontinued. The idea was to determine the frequency and size of the dose necessary to maintain mercury circulating in the body fluids, having assumed, as stated by Meyer and Gottleib, that the excretion of mercury in the urine offers a means of estimating the amount of mercury circulating in the body and that the success of the treatment depends on a certain amount of mercury in the body fluids. The effects of the various forms of mercury on the kidneys as determined by the appearance of protein, casts, or blood in the urine, was also to be estimated when possible.

Our first series of experiments were carried out according to the Elliot[6] method.

This series consisted of the following cases:

REPORT OF CASES

CASE 1.—Baby G., aged 2 weeks, was born with typical syphilitic lesions. A 1:1,000 mercuric chlorid solution was given, 10 drops, three times daily. Mercury was readily detected in the urine after the second day (not examined earlier). The mercury was discontinued and after one week the urine still contained traces. The urine, while this treatment was continued, contained appreciable amounts of protein and granular casts. The symptoms of syphilis rapidly cleared up under this treatment. Two months later, when having mercury ointment under the abdominal band, 0.5 gm. daily, appreciable amounts of mercury were found in the urine. May 17, two weeks after all treatment had been discontinued, distinct traces of mercury were found.

CASE 2.—Baby girl R., aged 5 days, had congenital syphilis. One gram of 33⅓ per cent. mercurial ointment was rubbed into the skin. On the second day mercury was readily detected in the urine and it is probable that it could have been detected earlier if examined.

CASE 3.—Baby boy L., newborn, was given 0.03 gm. of gray powder on December 5. On December 6, 7 and 8 mercury was readily detected in the urine.

CASE 4.—Edna B., aged 25 months, had congenital syphilis. She received 0.03 gm. of gray powder December 5. December 6, mercury was readily detected in the urine, also present December 8.

CASE 5.—Baby boy P., aged 4 days, was given 0.03 gm. of gray powder for three doses on the fourth day. On the sixth and eighth days mercury appeared in the urine.

CASE 6.—Baby girl R., aged 20 months, had congenital syphilis. She received seven inunctions of 0.5 gm. of 33⅓ per cent. mercury ointment before the urine was examined. Urine contained appreciable amounts of mercury.

CASE 7.—Baby boy J., aged 11 months, had congenital syphilis. He received two inunctions of 0.5 gm. of 33⅓ per cent. mercury ointment. Following the second inunction mercury was readily detected in the urine.

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[6] Elliot, J. A.: A New and Delicate Method for the Detection of Mercury, Jour. Am. Med. Assn., 1917, **68,** 1693.

RESULTS OF A SERIES OF EXPERIMENTS TO DETERMINE THE ELIMINATION OF MERCURY IN THE URINE

Name and Age	Diagnosis	Form of Mercury	Dose	Date of Treatment	Date of Examination	Amt. of Mercury in Mg.	Remarks
W. A. 21 months	Cerebrospinal syphilis	Gray powder and mercurial ointment	0.03 gm. 1.5 gm. every day for six days	2/22 to 3/8, inclusive	2/28	+	Appreciable amounts of protein in urine
					3/ 1	+	
					3/ 2	+	
				Gray powder discontinued, 3/8	3/ 3	+	
					3/ 7	0.44	
					3/ 8	0.97	
					3/12	+	
				Treatment discontinued, 3/26	3/26	+	
					3/28	+	
					3/29	+	
					4/ 2	+	Elimination of considerable amounts after periods during which there were only traces suggesting stored mercury in some organ
					4/ 8	1.5	
					4/ 9	0.2	
					4/10	+	
					4/12	+	
C. O. 9 years	Endocarditis; edema	Mercurial ointment	1.5 gm. 33⅓% mercury	3/19	3/19	+	
					3/20	+	
					3/21 to 4/5	—	
			1.5 gm. 33⅓% mercury	4/5	4/6	+	Note large amounts of mercury given and little elimination. Did the edema have anything to do with this lack of absorption?
			1.5 gm. 33⅓% mercury	4/6	4/7	+	
			1.5 gm. 33⅓% mercury		4/8	+	Discharged
E. B. 11 years	Congenital syphilis	....	......	....	4/18 and 21	—	Had had mercury long time before
		Mercury salicylate in oil	0.5 c.c. = 0.0325 gm. mercury salicylate	4/25	4/26	0.5	
					4/27	+	
					5/ 1	+	
					5/ 2	+	
					5/ 3	+	
					5/ 4	1.0	Appreciable amounts of protein in urine
					5/ 5	+	
					5/ 6	0.35	
		Mercury salicylate in oil	0.5 c.c. or 0.0325 gm.	5/7	5/ 8	0.5	Shows accumulation in system
					5/ 9	+	
					5/10	+	
					5/12	+	
					5/16	+	
					5/21	+	
B. 5 years	Congenital syphilis	Mercuric chlorid	1:1000 solution, 10 drops three doses only	4/10	4/11	+	
					4/14	+	
					4/26	-	
		Mercury salicylate in oil	0.5 c.c. = 0.0325 gm.	4/26	4/27	+	Appreciable amounts of protein in urine. A few granular and hyaline casts
					4/28	0.4	
					4/29	+	
					4/30	+	
					5/ 1	+	
					5/ 2	0.25	

RESULTS OF A SERIES OF EXPERIMENTS TO DETERMINE THE ELIMINATION OF MERCURY IN THE URINE—(*Continued*)

Name and Age	Diagnosis	Form of Mercury	Dose	Date of Treatment	Date of Examination	Amt. of Mercury in Mg.	Remarks
D. G. 10 years	Chorea minor	Calomel	0.016 gm. four doses	5/10	5/11	+	
					5/12	+	
					5/13	+	Bowels loose. Probably eliminated in feces
					5/17	+	
					5/18	+	
					5/19	+	
					5/20	+	
					5/21	+	
					5/22	+	
					5/23	+	
L. 9 years	Congenital syphilis; periostitis	Mercury ointment 50	1 gm. on knee and leg daily	Daily up to 4/10, discontinued 4/27	4/11	0.54	
					4/27	+	
					4/28	—	
		Mercury salicylate in oil hypodermically	0.5 c.c. or 0.0325 gm.		5/ 1	0.25	
					5/ 2	+	
					5/ 3	+	
					5/ 4	+	
C. N. 15 years	Congenital syphilis; periostitis	Mercurial ointment	1 gm. daily around knee	Daily	4/13	+	All treatment discontinued 4/13
					4/27	—	
		Mercury salicylate in oil	0.5 c.c. = 0.0325 gm.	4/27	4/28	+	Traces of protein in urine. Few casts
					4/30	+	
					5/ 1	+	
					5/ 5	+	
C. M. 3 years	Malnutrition	Mercury chlorid	0.5 c.c. of 1% solution hypod.	5/17	5/18	+	
					5/19	+	
					5/20	+	
					5/21	+	
					5/22-23	+	
F. O. 5 years	Burn; scar	Mercury chlorid	0.5 c.c. of 1% solution hypod.	5/17	5/18	+	
					5/19	+	
					5/20	+	
					5/21	+	
					5/22-23	—	
J. D. 5 years	Cystitis	Calomel	0.016 gm. for four doses	5/11	5/12	0.4	
					5/13	+	
					5/14	+	
					5/15	+	
					5/16	+	
					5/17	+	
					5/18	+	
					5/19	+	
					5/22	+	
Boy T. 1 year	Congenital syphilis	Calomel	0.016 gm. for four doses	3/14	3/15	..	This case had had mercury inunction for considerable time, but it had been discontnued two weeks before calomel treatment
				3/16		+	
				3/17		+	
				4/10		+	
G. C. 8 years	Diabetes mellitus	Mercurial ointment	1.5 gm. 33⅓% mercury	4/4	4/ 5	1.3	
					4/ 6	+	
					4/ 9	+	
					4/12	+	

Results of a Series of Experiments to Determine the Elimination of Mercury in the Urine—(*Continued*)

Name and Age	Diagnosis	Form of Mercury	Dose	Date of Treatment	Date of Examination	Amt. of Mercury in Mg.	Remarks
J. C. 6 years	Syphilitic periostitis	Mercurial ointment	1.5 gm. 33⅓% mercury	3/12	3/13	1.0	
					3/14	0.10	Approximately
					3/15	0.12	Approximately
					3/16	0.10	Approximately
					3/18	+	
					3/19	—	
					3/20	—	
Boy P. 2 days	Normal; newborn	Mercury salicylate in oil	0.5 c.c. = 0.0325 gm.	5/1	5/2	1.0	
					5/3	+	
					5/4	1.0	
					5/5	+	No further examination
Boy J. 2 days	Congenital syphilis	Mercury salicylate in oil	0.5 c.c. — 0.0325 gm.	5/3	5/4	0.3	
					5/6	+	
					5/10	+	Discharged
Boy M. 5 months	Congenital syphilis	Mercury ointment under band for past month	0.12 gm. mercury ointment	5/1 discontinued	5/2	+	Treatment discontinued
					5/9	0.75	
					5/16	+	

Several other new-born infants were given mercury by smearing 1 gm. of 33⅓ per cent. mercury ointment on a piece of linen and placing it in contact with the skin under the abdominal band (sealed with wax paper). Owing to the small amounts of urine collected, the results in some cases were unsatisfactory, but in many, positive traces of mercury could be demonstrated. All new-born infants left the hospital on the tenth or twelfth day.

FURTHER EXPERIMENTS

The next series of analyses were made by a modification of Heinzelmann's method.[7] It was necessary on account of the difficulty of securing chemically pure zinc, to substitute aluminum for zinc and dissolve in potassium hydroxid instead of hydrochloric acid. The method is as follows:

To the twenty-four-hour specimen of urine, usually not more than 500 c.c. are used, add 1 gm. of potassium chlorate and 5 c.c. of concentrated hydrochloric acid for every 100 c.c. of urine. Heat over the free flame until the color changes from dark red to light yellow. Cool to 70 C.; add 1 gm. of very fine granulated aluminum and allow to stand over night. Decant and wash twice with about 25 c.c. of water. Dissolve in 5 c.c. of potassium hydroxid, 40 per cent.; when solution is complete add 25 c.c. of concentrated hydrochloric acid. If solution is not complete after some time heat gently, cool, pour into a Hehner cylinder and dilute to 90 c.c. with water; add 10 c.c. of saturated hydrogen sulphid water, mixing with a glass rod, which is bent into a spiral at one end. At the same time prepare a standard, using equal amounts of aluminum, potassium hydroxid, and hydrochloric acid adding with a pipet 5 or 10 c.c. of mercuric chlorid solution containing 1 or 2 mg. of mercury. Compare colorimetrically. If the day's specimen of urine is less than 100 c.c., it is diluted to 100 c.c. and carried out as above; if the amount is more than 100 c.c. and less than 500 c.c., it is used without dilution.

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[7] Heinzelmann: Chem. Ztg., 1911, **35,** 724.

SUMMARY AND CONCLUSIONS

From the small series of experiments described in the foregoing charts we have drawn the following conclusions:

In infants and children, mercury, when given by the mouth, by inunction or intramuscularly, is excreted at least partly by the urine.

In new-born infants and older children mercurial ointment when placed in contact with the skin, without any friction being used (protected and sealed by wax paper from being volatilized and inhaled), is taken up by the skin and excreted in the urine and continues to be excreted in the urine for a variable time after all treatment has been discontinued.

By inunction (with rubbing) mercury is readily taken up by the skin and eliminated in the urine and continues to be eliminated for a considerable time.

When one inunction is given, the maximum daily amount of mercury is usually eliminated during the following twenty-four hours, smaller amounts being eliminated for a variable time.

Where continuous inunctions are given there is an accumulation in the system and considerable amounts are eliminated at intervals with only traces between.

It is therefore probable that it is unnecessary to have mercury in contact with the skin, either with or without rubbing as often or as long as has been generally thought necessary. This, however, must be determined by further clinical investigation.

Mercury salicylate suspended in oil and given subcutaneously continues to be eliminated in the urine in appreciable amounts for eight days, or longer, the daily amounts eliminated varying widely. It is therefore probable that a repetition of the treatment, not oftener than at intervals of eight days would be sufficient.

Mercuric chlorid by intramuscular method, a favorite method in congenital syphilis, continues to be eliminated for eight days or longer.

In all cases in which mercuric chlorid was used either by mouth or the intramuscular method protein was found in the urine.

Calomel, 0.016 gm. every two hours for four doses, and gray powder, 0.03 gm. every three hours for 3 doses, continued to be eliminated in appreciable amounts in the urine for as long as nine days; the maximum daily elimination usually occurred during the twenty-four hours following administration. It is therefore probable that the daily use of any of the mercurial salts in the amounts usually prescribed, is unnecessary and presumably harmful.

We shall continue our investigations and believe it is not too much to expect that in the near future, with the methods now at our disposal of estimating quantitatively the amount of mercury in the body fluids, some degree of accuracy will be attained in the treatment of syphilis by the different mercurial preparations.

We are grateful to Dr. J. P. Sedgwick, who suggested this problem, and for his constant interest in the work.

A CASE WITH VASCULAR, JOINT, MUSCLE AND SKIN DISTURBANCES OF UNCERTAIN ETIOLOGY *

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The subject of this report is a child, aged 4½ years. There are two other children in the family who are normal. The family history is in other respects negative.

CLINICAL HISTORY

This child was perfectly well and had no symptoms until early in November, 1917. At that time she was vaccinated against smallpox. The vaccine used was the same as that employed in many cases without any unusual results. The reaction from the vaccination was violent with high temperature and the involvement of the glands in the groin. A few days after the vaccination had subsided her face became red and swollen about the eyes and she complained of a little stiffness in bending her knees. From that time until early in January there was a steady progress in the condition, until at the present time all the joints of the body are involved including the spine. This condition is shown in Figure 1. Passive motion causes slight pain. It is impossible fully to extend or flex any of the joints. The feet are held in equinus position. The muscles feel as in chronic state of contraction. She does not voluntarily use even her hands. She is able to walk if compelled to do so, but stands on her toes and complains constantly to be put back to bed. The edema and redness about the eyes has persisted (Fig. 2). There have been subconjunctival hemorrhages. The mucous membranes of the mouth about the teeth are red, edematous and hemorrhagic in spots. In appearance they closely resemble the gums in scurvy. Under the arms a macular erythema appeared and progressed to the loss of the superficial layers of the skin in some places and has resulted now in brownish pigmentation (Fig. 3). There is also a larger area of a diffuse pink blush extending down almost to the crests of the ileum and to the anterior and posterior axillary lines. The fingers and toes show at their tips a blotchy erythema resembling Raynaud's disease (Fig. 4). The skin almost everywhere, but more marked on the legs, arms and back, presents a brawny induration. The superficial layers cannot be pulled away

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* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

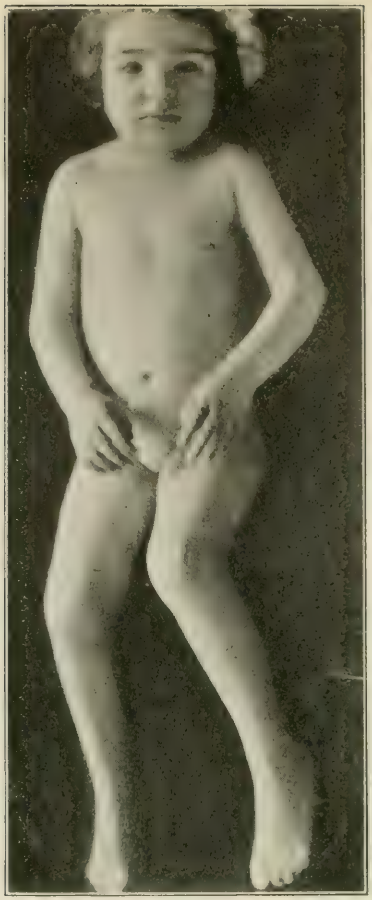

Fig. 1.—Showing the contractures which involved all of the joints of the body, including the spine.

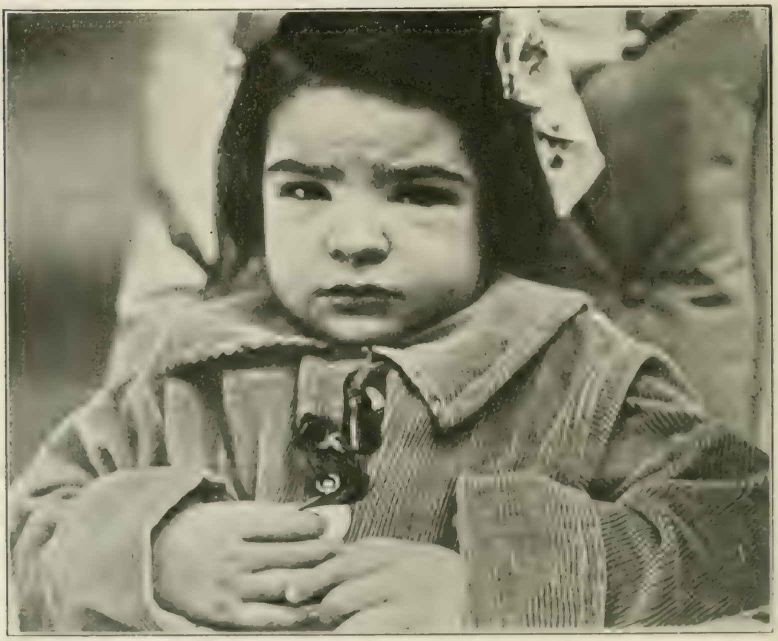

Fig. 2.—Edema with marked redness of the eyes and eyelids.

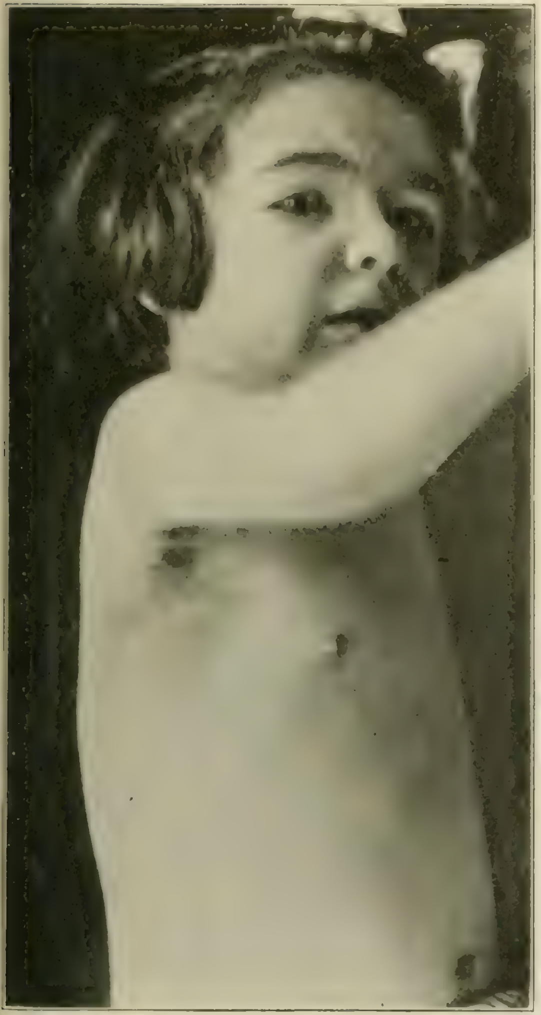

Fig. 3.

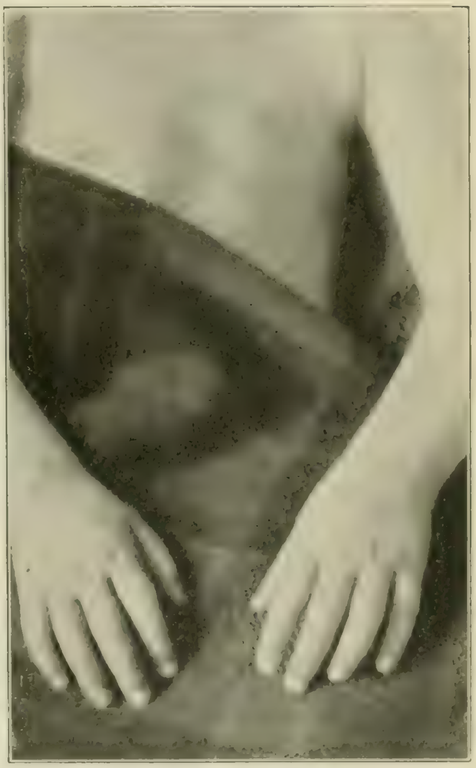

Fig. 4.

Fig. 3.—Pigmented and erythematous lesions in the axilla.

Fig. 4.—Blotchy erythema of the fingers and hands; a condition which resembles Raynaud's disease.

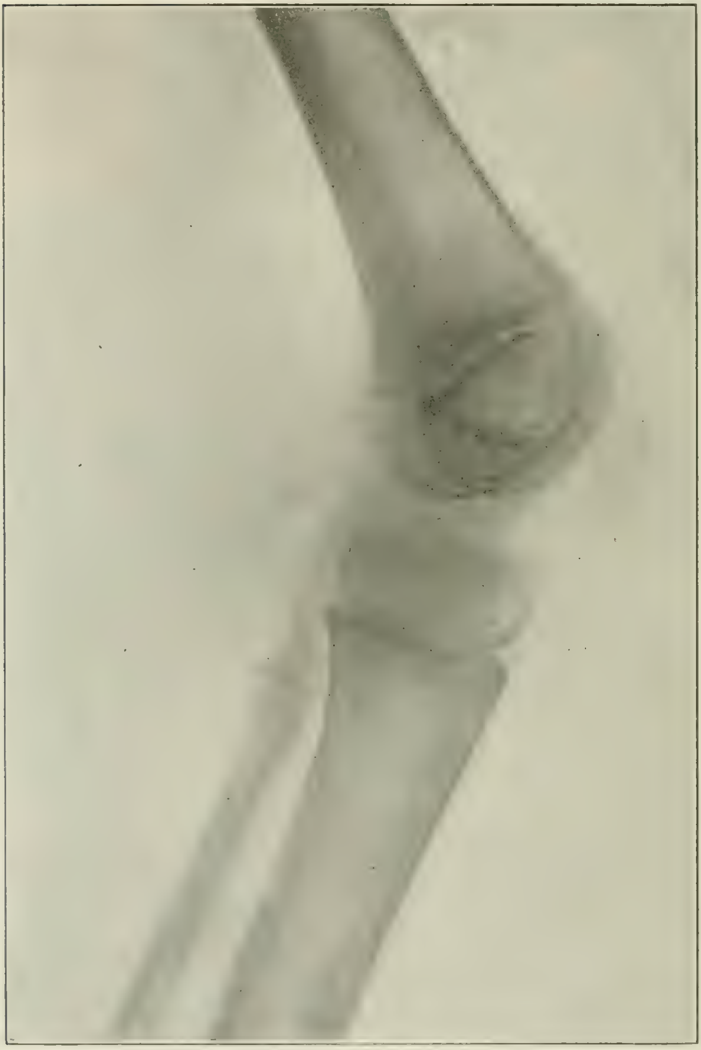

Fig. 5.—Roentgenogram of the knee joint which reveals nothing pathologic, peculiar skin condition seen in plate not visible in print.

from those beneath. In some portions, especially over the sacrum, there is slight edema. The lesions of every kind are absolutely symmetrical even to the position of the erythematous blotches on the finger tips. The skin feels a little dry, but perspiration is present. The hair is rather coarse, but abundant even on the upper portion of the back and on the arms. Previous to the onset of symptoms the child was cheerful and happy, but since the trouble began she has become very tearful, quiet and does not want to be disturbed.

PHYSICAL EXAMINATION

Aside from the lesions mentioned, the physical examination is entirely negative. There has been no fever. The blood is normal. The urine is normal except that in the last two weeks there have appeared a few pus cells and coincident with this a slight rise in temperature. The stool is negative, except at first there was a slight excess of starch. The blood pressure is normal. The pulse rate is 120. The Wassermann test is negative. The Von Pirquet test is negative. The blood culture is negative. The roentgenogram reveals nothing pathologic in the joints (Fig. 5). The sella turcica is normal. The teeth are normal. The subcutaneous tissues show a curious irregular striation unlike anything with which we are familiar.

SUMMARY

The striking features of this case are as follows: The very extensive symmetrical involvement of various portions of the body, the brawny induration of the skin, the vascular disturbance of the skin and mucous membranes, the stiffness of the joints, the roentgen-ray findings in the skin, and the change of disposition.

The etiology of this condition is extremely doubtful. We believe that the vaccination had nothing to do with it. Possibly some toxic agent has affected the glands of internal secretion. No focus of infection has been found. Some change in the vascular system is suggested by many of the findings. The skin may be primary and the other signs secondary to it. The most likely diagnosis seems to us to be a diffuse scleroderma.

So far as treatment is concerned, nothing has been done which has modified the course of the condition in any way. In the last three months there has been very little progression, and in the last few weeks there has been a slight tendency toward improvement.

MIGRAINE IN CHILDHOOD*

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While migraine in later childhood differs in no respect from the disease as seen in the adult, its recognition in infancy and early childhood offers considerable difficulty, owing to the inability of the patient to describe symptoms accurately.

As is well known, migraine is often a hereditary disease, being directly inherited in about 50 per cent. of the cases. Not infrequently it has been known to occur in three or even four generations. It has not yet been ascertained whether or not the mendelian laws govern its inheritance. Like other hereditary diseases, it may be congenital, though this is exceptional. Such was the case with Russell's patient,[1] who had the first manifestations at the age of 2 weeks, with attacks regularly thereafter every two weeks; at the age of 7 years the disease changed to the ophthalmoplegic type.

Age at Onset.—In Flatau's[2] large series of 307 cases, the disease began most frequently from the sixteenth to the thirtieth year, but in 21 per cent. the onset was before this period and in 12 per cent. before the eleventh year. In only 1 per cent. did it begin during the first five years of life. Gowers,[3] however, found a larger incidence in childhood, about one-third of his cases beginning between the fifth and tenth years, and two-fifths between the ages of 10 and 20. All writers agree that it is rare in the first half decade.

Symptomatology.—In infancy the symptoms are obscure and the attacks are of shorter duration than in the adult, lasting only a few hours. There are periodic attacks of vomiting, associated with pain and restlessness, and sometimes convulsions; the temperature is often somewhat raised. Constipation is the rule, in contrast with gastroenteritis, a disease which is in other respects somewhat similar to migraine at this period of life.

In early childhood the attacks are more like those in the adult, though the pain is less often localized in one side of the head, and sensory and ophthalmic symptoms are less common. Of great interest is the association with cyclic vomiting, which is apparently not very

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* Submitted for publication Aug. 26, 1918.

* Read at the meeting of the American Pediatric Society, Lenox, Mass., May 28, 1918.

[1] Russell, J. W.: Brit. Med. Jour., 1903, **1,** 1020.

[2] Flatau, E.: Die Migräne, Berlin, 1912.

[3] Gowers, W. R.: Diseases of the Nervous System, Ed. 2, 1898, **2,** 836.

uncommon. Usually cyclic vomiting appears first and is replaced later in childhood by migraine, but in the case of Comby[4] migraine appeared at the age of 2, and was replaced by cyclic vomiting at the age of 8, while in one of Fabre's[5] cases, a girl of 9, migraine came first, but did not cease with the appearance of cyclic vomiting.

The association with epilepsy is rare in childhood.

Increased intestinal putrefaction is a rather frequent accompaniment of migraine which is often overlooked. While it is not constant, and therefore cannot be the cause of the disease, it appears to aggravate the attacks, and hence is worthy of consideration. The examination of the urine for phenol will often reveal such putrefaction where the test for indican is negative. It cannot be too strongly emphasized that the amounts of phenol and of indican in the urine are quite independent of one another. The reason for this is that phenol is derived from the tyrosin portion of the protein molecule, while indican is derived from tryptophan. It is possible that one set of intestinal micro-organisms attacks tyrosin, and another tryptophan. A simple test for phenol in the urine is the following: 100 c.c. of urine are distilled with 5 c.c. of strong sulphuric acid until one-half of the liquid has gone over, and to the distillate is added bromin water in excess. The presence of a definite white precipitate (tribromphenol) indicates the presence of phenol in excessive amounts.

Recent work by Folin and Denis[6] and by Dubin[7] has thrown new light on the physiology of the phenols. This has been rendered possible by a new colorimetric method, devised by Folin and Denis,[8] by which phenol, both free and combined, can be determined rapidly, and with accuracy. Contrary to the long-prevailing opinion, Folin and Denis have shown that the greater part (about 80 per cent.) of the phenol in the urine is normally excreted in the free state. Dubin, however, found that if phenol is administered in large amounts to dogs, a very marked increase in the conjugation takes place. It would appear, therefore, that the protective mechanism by which phenol is rendered harmless is called into play only when excessive amounts have to be cared for. The total amount of phenol, both in animals and in man, was found to vary directly but not proportionally with the intake of protein. After the use of enemas and of cathartics the amount is lowered appreciably.

The nature of migraine is still little understood. The analogy with epilepsy is very close; in both conditions there is a strong hereditary element; in both periodic cerebral attacks, affecting in the one case the sensory, in the other the motor sphere. Moreover, the two diseases often have been found in the same person, migraine occurring first, being replaced later by epilepsy.

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[4] Comby, J.: Arch. de méd. d. enf., 1901, **4,** 9, Observation 11.

[5] Fabre, E.: Migraine chez les enfants. Thèse de Paris, 1904.

[6] Folin, O., and Denis, W.: Jour. Biol. Chem., 1916, **26,** 507.

[7] Dubin, H.: Jour. Biol. Chem., 1916, **26,** 69.

[8] Folin, O., and Denis, W.: Jour. Biol. Chem., 1915, **22,** 309.

A comparison with asthma, another hereditary disease, suggests another point of view. Here again are periodic attacks, with intervals of good health. The symptoms of asthma resemble closely those of anaphylactic shock in the guinea-pig, and for many cases a hypersusceptibility to certain proteins has been demonstrated. It has been attempted to explain migraine also as a manifestation of anaphylaxis, but thus far without success. It is true that indiscretions in diet may precipitate an attack of migraine, and that a low protein diet is beneficial in some, though by no means in all cases, but hypersusceptibility to proteins has not been shown by direct methods, eosinophilia has not been reported, and the symptoms are not similar to those of experimental anaphylaxis.

A disorder of metabolism is another possibility, for which there are analogies among inherited diseases, such as diabetes and gout, in which there is direct heredity, and those rare anomalies of metabolism, pentosuria, cystinuria and alkaptonuria, in which, however, the condition is congenital and familial but not hereditary. Moreover, diseases of metabolism may show marked periodicity, as in gout, and that rare disease known as family periodic paralysis, in which Edsall and Means[9] have recently shown decided disturbances of metabolism, in the shape of increased basal metabolism during attacks, and a long continued marked increase of the nonprotein nitrogen of the blood, in the absence of nephritis. Very little work has been done on the metabolism in migraine, and this should offer a good field for future investigation.

It often has been attempted to explain the symptoms of migraine on the basis of an abnormal reaction of a diseased central nervous system to stimuli which in the healthy person would produce no effect. In favor of this view various signs of a disturbed vasomotor and sympathetic innervation during the attack have been adduced. But this theory altogether fails to explain the most striking feature of migraine, namely, the periodicity of the attacks, and the sense of well being during the intervals.

To sum up, the cause of migraine remains obscure. The hypothesis of intoxication by the products of a disordered metabolism seems at present to offer the best basis for investigation.

Diagnosis.—The diagnosis rests chiefly on the periodic occurrence of headache, accompanied usually by nausea and vomiting. The intervals between attacks vary from one to two weeks up to several months in duration, and are free from symptoms, unless the attacks follow one another very closely. It is not essential that the headache should be confined to one side; in case it is not, it is usually frontal, rarely occipital. Scintillating scotomas, numbness of one side of the body and other ophthalmic and sensory symptoms are not a necessary part of the disease, and in fact are rare in childhood. A family history of migraine is of much diagnostic value. In young children the diagnosis may be difficult on account of their inability to describe symptoms. The periodicity of the attacks, however, and the state of well-being between them, together with the exclusion by careful physical examination, of other causes of headache, will usually enable one to arrive at the correct conclusion.

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[9] Edsall, D. L., and Means, J. H.: Am. Jour. Med. Sc., 1915, **150,** 169.

From cyclic vomiting it is differentiated by the following features: in migraine the headache precedes the vomiting, and is the predominating symptom, while in cyclic vomiting the headache is usually not severe, and the vomiting is frequent and intractable. The presence of large amounts of acetone in the urine is constant in cyclic vomiting, and also in migraine providing vomiting is present, but in the former it may precede the attack, and in that case has diagnostic value.

Treatment.—A thorough examination of the patient, with especial attention to the eyes, nose, throat, accessory sinuses, teeth and digestive tract, is a prerequisite of intelligent treatment. While it is doubtful if true migraine has ever been cured by the correction of refractive errors, of nasal troubles or by alterations of the diet, it is true that any measure that improves the patient's general condition is likely to ameliorate the severity of the attacks, and to reduce their frequency. For this reason any abnormalities which are capable of correction should receive attention.

The diet is of considerable importance. It is well known that some persons have fewer attacks if meat and fish are excluded. This effect was formerly attributed to the influence of a purin-poor diet on the uric acid diathesis, which was erroneously supposed to play an important part in migraine. It may well be due to the reduction of an increased intestinal putrefaction, a factor which should always be looked for. If it is present, meat, fish and eggs should be excluded from the diet, and the effect on the excretion of phenol and indican noted. In some cases it may be even necessary to exclude milk to attain the desired result. Constipation, if present, of course should be corrected, as tending to increase intestinal putrefaction.

In a few cases attacks apparently are precipitated by overindulgence in corbohydrates, such as candy.

Attention to hygiene is an essential part of the treatment. It is often necessary to withdraw the child from school for a while, and to limit the hours of study and reading. An abundance of fresh air and exercise in amounts suited to the individual are indicated.

The use of drugs during the attack should be limited, since in small doses they have no effect, and in large doses they are apt to be deleterious. Of the antineuralgics, caffein seems to have the best effect. Morphin may be required in very severe paroxysms. The administration of drugs during the intervals, with the purpose of reducing the severity and frequency of attacks, has proved disappointing in my hands, though recommended by Oppenheim and other authorities.

By the use of the above measures the frequency and severity of the attacks are usually lessened, but it is doubtful if true migraine is ever cured.

The following case seems worthy of report on account of the unusually early incidence of the disease and the presence of large amounts of phenol in the urine.

REPORT OF CASE

History.—H. B., a boy, aged 6 years, was seen March 1, 1918, in consultation with Dr. H. M. Steele.

Family History.—The maternal grandmother and a maternal aunt have suffered severely from typical migraine. The parents and a sister aged 4 years are free from headache.

Past History.—This is negative except for the fact that as an infant he used to lick the paint off the bed.

Present Illness.—Since the age of 3 years, he has been subject to periodic attacks of headache, accompanied by vomiting. Acetone occurs abundantly in the urine at these times, a feature which had led to the diagnosis of cyclic vomiting. The attacks come at intervals of from one to three months, as a rule, but during the previous winter have occurred about once a week. There is an aura the day before, consisting of pallor, nervousness and an abnormal appetite, usually poor, but sometimes increased to a pathologic degree. The headache is intense and always precedes the vomiting; it is bilateral and frontal in distribution and accompanied by photophobia. The duration of the attack is about twenty-four hours. Between attacks the boy is well and free from headache. There has been a distinct intolerance of eggs; if he takes more than one egg a week he is almost certain to have an attack. He has not taken large quantities of meat.

Physical Examination.—A fairly developed boy, 45 inches in height, weighing only 37 pounds (the normal weight for this age is 45 pounds). The head is rather square, but there are no other signs of rickets. The tonsils are moderately enlarged. The heart, lungs, abdomen and reflexes are negative. The systolic blood pressure measures 82 mm., the diastolic 50. The examination of the eyes by Dr. E. M. Blake, shows a considerable degree of hypermetropia (+2 D.). The hemoglobin is 90 per cent. The blood smear shows a considerable increase in lymphocytes, the count being as follows: polynuclear nuclears, 35 per cent.; lymphocytes, 58.5 per cent.; large mononuclear and transitional cells, 4 per cent.; eosinophils, 1 per cent., and mast cells, 1.5 per cent. The red cells are normal.

Urine: Twenty-four hour amount, 500 c.c., color normal, reaction acid, specific gravity 1.015, albumin sugar and indican absent, *phenol present in large amounts,* acetone present (during the attack), sediment negative. Examination of the feces for lead is negative.

Treatment.—The treatment consisted in withdrawal from school, the correction of the refractive error and alteration of the diet. Throughout the month of March no meat or fish was eaten. During April the child was put back on his former diet. It was now found that he had an increased tolerance for eggs, which he craves, being able to take three or four a week without headache. Examination of the urine April 16 and May 22 still showed large amounts of phenol; during March, when the protein intake was restricted, no examination was made. In spite of the phenoluria he has been practically free from headache since beginning of treatment, having had but one slight attack from March to the date of writing, June, 1918.

COMMENT

The beneficial effect of even a temporary diminution of the protein intake is shown in the almost complete disappearance of the headaches, and in the increased tolerance of eggs. Further restriction of protein is indicated, until the excretion of phenol reaches normal limits.

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PROGRESS IN PEDIATRICS

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF CHILDHOOD*

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In surveying the literature of the past year in these fields one's attention is caught by the notably large number of contributions that deal with problems of nutrition in childhood, by the number of articles on hypertrophic stenosis of the pylorus in infancy, and by the unusually large number of fetal anomalies that are reported.

That there should be numerous articles dealing with problems of nutrition is but natural and is a reflection of the importance of the subject in a time of changing and often restricted dietaries. Careful study of all the conditions surrounding infancy and childhood, birth, nutrition and growth, is stimulated by the insistent call for men that comes from all the warring nations. It is clear that if there are to be healthy, efficient men in the future, there must be well-born, well-nourished infants, in the present.

PHYSIOLOGY

Birth Rate.—In his address as a retiring sectional vice president of the American Association for the Advancement of Science, Louis I. Dublin,[1] statistician of the Metropolitan Life Insurance Company, discusses in an able manner the significance of the declining birth rate. The condition is not peculiar to any one nation. It affects not only the gross totals of population, but also the internal structure of population. In the presence of a declining birth rate, youth and strength come to form a smaller part of the total population, the old and dependent form a much larger part. Moreover, the reduction of birth rate is found to have affected mostly those who are both economically and socially best fitted to bear and to raise a family.

In order that a national stock may maintain itself without increase or decrease it is found that the average number of children in the family must be close to four. At first thought it might seem that something over two children per family would suffice to maintain the stock. That this is not true is due to three facts: (1) not all persons marry; in America, 12 to 15 per cent do not marry until after the reproductive period, if at all; (2) a considerable proportion of marriages, over 7 per cent., are sterile; (3) the death rate is exceptionally high in the period of childhood, amounting in the first year of life to about 10 per cent. of the babies born, and continuing, at diminished rates, until at the average age of marriage there are only 73,000 individuals left out of every 100,000 born.

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* Submitted for publication Sept. 26, 1918.

[1] Tr. Am. Assn. for Advancement of Science, 1918.

From a national point of view the situation in America is made worse by the fact that it is the native stock that is declining. A tabulation based on the population returns of the 1910 Census shows that while in a group of women under 45 years of age who were married for a period of ten to twenty years the average number of children was 4.1 per married woman, the woman of native parentage showed an average of only 2.7 children per married woman. Moreover, the women of native parentage had borne no children in 13 per cent. of the cases, the women of foreign parentage in only 5.7 per cent. of the cases.

Among our college bred women the number of children per married woman is strikingly small—Smith College, 1.3; Vassar, 1.6; Bryn Mawr, 1.7; Holyoke, 1.8; figures that are all the more significant since less than 50 per cent. of the graduates of women's colleges marry. Studies of the families of 643 American men of science by Cathell, show that these men came from families that had an average of 4.7 children; their own families, where the men were married and their families were complete, showed an average of only 2.3 children, these figures including all the children born.

It is clear that this decrease in our national stock is due to the exercise of conscious limitation of births. Our national stock is being replaced by a stock of a different order. Our national standards, says Dr. Dublin, are being leveled to meet more and more the lower quality of our population.

The matter is one that vitally concerns the individual and the society of individuals, the state. It is suggested that the state may lessen the evil by providing a more rational education, by inculcating national ideals, by making our various national groups conscious of their best traditions and instilling desires to see their better strains strengthened and increased as a foundation of the greater democracy of the future.

The economic and social burden that is now laid on the man and woman who bears the requisite number of children must be lessened. The mother of several children should be favored with the admiration of the community in which she lives, not with its commiseration and pity. It may be found expedient for the state to encourage parenthood by considering the size of the family, as a factor, among others, in fixing exemptions from taxes. The need of conscious and deliberate birth release among the healthy and normal people of the country is emphasized as primary national duty.

Hamill[2] points out that in every warring country the number of children will continue to decrease in proportion to the number of men called to arms, the number of women taken into industry, and the increase of price in the essentials of life. The various nations face (1) a decreasing birth rate; (2) increasing death rate, and (3) an appalling destruction of adult life in the field of battle. Thousands of men will be totally incapacitated, many more thousands will be only partially capable in years to come. Death and wounds from battle can not be materially lessened so long as the war continues; an increase in the birth rate in war time is not possible; the one possible solution lies in so reducing the infant death rate as to, at least in part, compensate for the loss of population that the other conditions are producing. The attention of nations is thus focused on the available means of saving infant lives. By rendering her governmental agencies more efficient, by increasing her health visitors to one to every five infants born, by granting votes of money to private welfare agencies, so that instead of curtailing they might extend their work, England reduced her infant death rate for 1916, to 91 per thousand living births, a saving over the former year of over nineteen lives in every thousand born. England then was able in 1916 to compensate in a large part for her decreasing birth rate. Hamill estimates that in Pennsylvania alone it would be possible to save about 6,000 babies' lives yearly. A definite health campaign that will carry the necessary information directly to the mothers seems to be the most effective means of combating infant mortality.

Beitler[3] cites Karl Pearson's estimate that for every 1,000 liveborn children, there are 605 stillborn. Mall believed (personal interview) that the incidence of stillbirths is at least one-half of the total number of live births. He says that "out of 58,089 deaths under one month in the registration area in 1910, 25,672, or 61.40 per cent., were attributed to antenatal causes." It is axiomatic that the cause of the mortality from the first to the eleventh day of life is determined almost entirely by prenatal causes.

Birth, Weight and Growth.—Warren[4] reports that in 2,000 con-

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2. Hamill, S. McC.: Influence of War on Infant Mortality and Its Meaning, Am. Jour. Med. Sc., 1918, **155,** 1.

3. Beitler, F. V.: Reduction of Infant Mortality Due to Prenatal and Obstetric Conditions, Am. Jour. Obst., 1918, **77,** 481.

4. Warren, S. P.: Average Birth Weight in 2,000 Confinements. Am. Jour. Obst. and Dis. Women and Child., 1917, **76,** 932

finements occurring chiefly in his private practice (State of Maine, 1874 to present time) the average birth weight has been 8¼ pounds for girls, and 8¾ pounds for boys. The mothers belonged to every grade of life, both rich and poor. The average weight of children of foreign born mothers exceeded that of native born American mothers by four-tenths of a pound. It is Warren's experience that babies weighing 10 or 12 pounds at birth are quite frequent in Maine, a condition possibly explained in part by the fact that the state abounds in men and women of large stature, though this would not apply to the foreign element. Balantyne (Antenatal Pathology) says: "The factors of fetal nutrition are so numerous and their relations are so intricate, that it is impossible to arrive at the coefficient of nutrition, so to speak."

Hammett[5] studied the relation between weight at birth and early growth as shown in 537 infants. The data were collected from the records of the Boston Lying-In Hospital, and showed the weight of the infants on the first, third, fifth, seventh, ninth, eleventh and thirteenth days after birth, excluding from consideration those whose food supply was derived either wholly or in part from sources other than the maternal breasts. The infants studied were divided into groups: one hundred infants weighing 5 to 6 pounds, one hundred 6 to 7 pounds, etc. The results recorded in the paper are based on the weights at birth.

The postnatal per cent. loss was found to vary directly with the weight at birth. With the exception of the heavier infants, the third day after birth marked the beginning of the pick-up to the normal rate of growth characteristic for the individual groups. After the third day the per cent. additions to the initial birth weight made between successive weighings shows a steady increase, and one that is greater in the case of the smaller infants.

Hammett[6] points out that Osborne and Mendel, McCollum, and others have shown that the nature of the food ingested is one of the very important factors concerned in growth, that no experimental evidence has yet been presented in support of a theory that the milk elaborated by a mother is not that biologically adapted to the needs of the young of the same species, and that any attempt to determine the fundamental biologic laws of growth during early infancy should recognize this. The factors influencing milk production are manifold. The nutritive condition of the mother, the maternal metabolism, health or disease, all contribute their quota. Nevertheless, during the first two weeks of lactation the variations in the chemical composition of human milk have a remarkably uniform tendency, "and where changes in the weight of the infant do not indicate supplementary feeding necessary, it can reasonably be assumed that the nourishment is sufficient and characteristic."

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[5] Hammett, F. S.: Relation Between Weight at Birth and Growth Capacity. Am. Jour. Physiol., 1918, **45,** 396.

[6] Hammett, F. S.: Jour. Biol. Chem., 1917, **29,** 381.

As the result of his study the author offers the following conclusions:

> The growth capacity of human infants during the first two weeks after birth is in a large degree dependent on the weight at birth. It is roughly inversely proportional to the initial weight. The ability to recover and pass the initial weight after the postnatal decline obviously varies in the same way, so that at the completion of the period studied (first thirteen days after birth) some 82 per cent. of those infants weighing between 5 and 6 pounds at birth have recovered or passed their initial weight, as compared with 20 per cent. of those weighing from 10 to 11 pounds. The intermediate groups vary inversely as to their weight at birth.

The result of a study by Camerer[7] seems to indicate that differences in growth are similarly correlated with differences in inital weight throughout a much longer period, for he found that in a series of 138 cases, divided into three groups, according as they weighed under 2,000 gm. between 2,000 and 2,750, and over 2,750, and studied after weekly weighings, that the percentage increment of the subjects in the first group was 427, of the second 219, and of the third and heaviest only 195.

It may be noted in passing that 65 per cent. of the infants in Hammett's series weighed between 6 and 8 pounds at birth—30.3 per cent. between 6 and 7 pounds—34.7 per cent. between 7 and 8 pounds. Numerous references to the theoretical aspect of the subject are embodied in this paper.

Bleyer[8] quotes from recent authors to the effect that while we now possess a fairly accurate and extensive knowledge of the normal curve of growth of certain animals, particularly the white rat and white mouse, we are not yet in possession of equally reliable and extensive data concerning the growth of human beings. The most important contribution on periodic acceleration and retardation of growth in children is doubtless that of Malling-Hansen.[9] This study was preceded by the work of Fleischmann, Vierordt, and, particularly, Camerer, and followed by that of Vahl, Buffon, and Godin. Malling-Hansen was able to divide the year into three periods which seemed to him quite well defined. A period of minimal growth was found to occur between mid-April and mid-July, a period of maximal growth between mid-July and mid-December, and a period of mean growth, the so-called "rest period," from mid-December to mid-April. The differences between these were found to be very great, growth in the maximal period being twice or even three times as great as that in the minimal period.

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[7] Camerer: Jahrb. f. Kinderh., 1901, **53,** 281.

[8] Bleyer, A.: Periodic Variation in Rate of Growth of Infants. Arch. Pediat., 1917, **34,** 366.

[9] Ueber periodic Gewicht des Kindes. Copenhagen, 1883.

Bleyer made a simple tabulation of the weights of 1,000 babies who attended a conference for well babies in St. Louis. Records were selected of infants showing normal temperature on the day of weighing, and an absence of recorded illness, both on the day of weighing and the next preceding visit to the conference. Because of the need of dealing with the well babies, no records were used which showed a loss of weight. Half the infants were in the first year of life, and half in the second. Altogether 3,800 weighings were tabulated; they were fairly evenly distributed through the various months of the year and were collected through a period of five years.

The gains were averaged on a basis of grams per day and then transferred for greater convenience into grams per week. Charts were prepared showing the average weekly gains, month by month, of infants in their first, and infants in the second year. A definite seasonal variation is seen. In the second year where the variations were much more marked a definite coincidence with the findings of Malling-Hansen is seen. In the first year the variations were not very great, though sufficient to show the rule. It was found that they were less marked in breast fed infants than in those that were artificially fed.

Following the division into periods suggested by Malling-Hansen, it was found that in the second year the average weekly gains from April to July were 77 gm.; from August to November, 113 gm.; from December to March, 86 gm. These and the preceding figures are presented in tabular form.

No scientific support was found for any of the various hypotheses that have been advanced to explain the phenomenon of periodic variation in the rate of growth. The view that the acceleration is due to change of diet would not seem to apply to infants, because in the first year no change is usually made, nor is the diet largely different in the summer in the second. It is noted that St. Yves Ménard and also Cornevin observed acceleration in the rate of growth in cattle in summer and fall, and found that this occurred independently of a change in diet.

The following conclusions are offered:

First, periodic variation in the rate of growth, consisting of an acceleration from midsummer to late fall, a retardation in winter and greater retardation in spring and early summer, was found to exist among infants.

Second, this would not appear to be due to change of diet.

Third, weight gains in the first year of life were greater in summer and fall than in winter and spring, and in the second year of life the best gains were made in August, from which it would not appear that heat has a retarding effect on the rate of growth, but may even favor it.

Fourth, it would seem that the external factors of growth may have to be taken into account in constructing normal weight curves for the first and second years of life.

Anthropometric photographic control of children's growth is discussed by Jeanneret and Messerli.[10]

Metabolism of the New-Born.—Talbot[11] points out that while there has been an increasing amount of investigation of the metabolism of the new-born infant during the past few years, only recently has enough evidence been accumulated to be of any practical value to the general practitioner. Discussion of the subject requires clear understanding of some technical terms, such as "basal metabolism," "respiratory quotient," "energy requirements," etc.

Basal metabolism, as defined by Talbot, means the energy production of an infant in complete muscular repose. It may be obtained only when the baby is asleep. Ideally it should be determined when the stomach is empty, but this is rarely possible in infants, as they usually sleep only when the stomach is full.

The *respiratory quotient* means the volume of carbon dioxid expired, divided by the volume of oxygen used. It has been found that when pure carbohydrate is burned up outside the body the volume of oxygen necessary for its combustion is always the same as the volume of carbon dioxid given off as the result of the combustion; the respiratory quotient of carbohydrate is therefore 1.00. The respiratory quotient of fat is 0.713 and of protein 0.801. Tables have been made from which the amount of the different food components that are being burned up in the body may be estimated, for each respiratory quotient. For example, when a respiratory quotient is 0.90, two-thirds of the energy used up comes from carbohydrate and one-third from fat.

The *energy requirements* of an infant, for example, is the amount of available energy expressed in terms of calories per kilogram required by the body to maintain the vital activity and keep the body warm. The *basal energy requirement* is the amount of energy, again expressed in calories, required to meet the needs of an infant in a state of complete muscular repose; that is, to meet the needs of basal metabolism.

Talbot finds that the *basal* energy requirement of infants from one-half to 6 days of age is 44 calories per kilogram of body weight, whereas the average of a 4 to 5 months old infant is in the neighborhood of 55 calories. The actual requirement for a new-born baby is approximately 62 calories per kilogram of body weight. The requirements rise as he grows older, continuing to do so until about the third month, and then diminishing. Energy production in the form of body heat is a large factor in determining the requirements. The amount of heat produced depends on the amount of *muscle* and the "active protoplasmic tissue" in the body. The presence of a large amount of fat, an inert tissue, so to speak, diminishes the heat production per unit of body weight. The low requirement of the newborn infant is probably related to the disproportionately large amount of fat present in the body of the normal infant; as he grows muscles begin to replace the fat and come to represent a larger proportion of the body weight.

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[10] Jeanneret, L., and Messerli, G.: Anthropometric Photographic Control of Children's Growth. Rev. méd. de la Suisse romande, 1917, **37,** 570.

[11] Talbot, F. B.: Physiology of New-Born Infant. Am. Jour. Dis. Child., 1917, **13,** 495.

The basal metabolism may also be calculated per square meter of body surface (determined, for example, by Lissauer's formula), or as total heat per twenty-four hours. Talbot finds that shorter infants produce less heat per square meter of body surface, than do longer infants, after the first day and a half of life. He divided the heat production per square meter of body by the length of the infant, and the average of the resultant figure was 12.65 calories. Taking the figures as a constant he offers the following formula for determining the energy requirements:

Total calories = length × 12.65 × body surface.

The earliest study of the respiratory metabolism of the new-born infant— it is from the respiratory metabolism that Talbot calculates the energy metabolism—was made in 1877 by Forster.[12] The most important subsequent investigations were published in Danish (Hasselbach, 1904) in such inaccessible form that they were overlooked. They have recently been translated into English and published by the Carnegie Institute of Washington.

The new-born infant does not receive food enough to supply the necessary energy to keep it warm. The body utilizes the glycogen stores of the liver and tissues. This is soon exhausted and the energy is then obtained from the body fat. The destruction of the body tissue contributes to the so-called physiologic loss of weight, part of which is mechanical and part truly physiologic. Anything that protects the infant from unnecessary loss of heat on the one hand, or that supplies a satisfactory source of energy on the other hand, should diminish this loss. Talbot suggests the omission of the routine bath, substituting a cleansing of the body with warm oil, and advocates the feeding of weak or premature infants with breast milk, or, when this is lacking, with temporary feeding of a 5 per cent. solution of some sugar such as lactose.

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[12] Forster: Amtlicher Bericht der 50 Versammlung deutsche Naturforscher u. Aerzter in München., Munich, 1877, p. 355.

Murlin[13] criticises this in saying that fat does not replace active tissue, but replaces water. "Hence we are driven back on the old explanation which Rubner himself gave, namely, that the lean infant has the higher metabolism because he loses heat faster. He has a larger surface in proportion to weight, and, since it is through surface that heat is lost, it will be in proportion to surface that heat must be produced if the body temperature is to remain constant."

Nutrition in Children.—In a recent article on "The Fundamental Requirements of Energy for Proper Nutrition," Graham Lusk[14] points out that our knowledge of different portions of the subject varies greatly in accuracy. Certain portions of our data "are matters of established fact, repeatedly confirmed; others are based on unconfirmed observations of individual authorities, but probably correct; while still others are based on estimates as close to the actual state of affairs as one can now attain." Our data on basal metabolism of all ages and sexes may be regarded as absolutely accurate, as also, the increase in metabolism due to (*a*) standing; (*b*) walking; (*c*) carrying a load (in adults). On the other hand, our data on the metabolism of children during exercise is to be classified as hypothetic.

Graham Lusk presents a table (Table 1) showing the metabolism of boys from birth to 16 years of age. The curves are based on data for the child at birth (Bailey and Murlin, Benedict and Talbot[15]); data showing a basal metabolism of 48 calories per kilogram of body weight for boys of from 6 to 12 months (Murlin and Hoobler[16]); 60 calories per kilogram for boys of 2 years (Magnus-Levy and Falk's[17] report on the metabolism of a boy 2½ years weighing 11.5 kg.); boys of from 6 to 16 years as shown in curves by Du Bois[18] and in the data showing that boys of 12 years have a basal metabolism of 50 calories per square meter per hour, and at 14 years of 44 calories for the same unit of measure. The metabolism of girls has never been investigated.

As presented in the table the amount of food expressed in terms of total available calories that must be supplied to meet the demands of basal metabolism (see foregoing definition) rises rapidly until the end of the second year, when it reaches 800 calories for a child weighing

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[13] Murlin, J. R.: Metabolism of Mother and Offspring Before and After Parturition. Am. Jour. Obst., 1917, **75,** 913.

[14] Lusk, G.: Jour. Am. Med. Assn., 1918, **70,** 821.

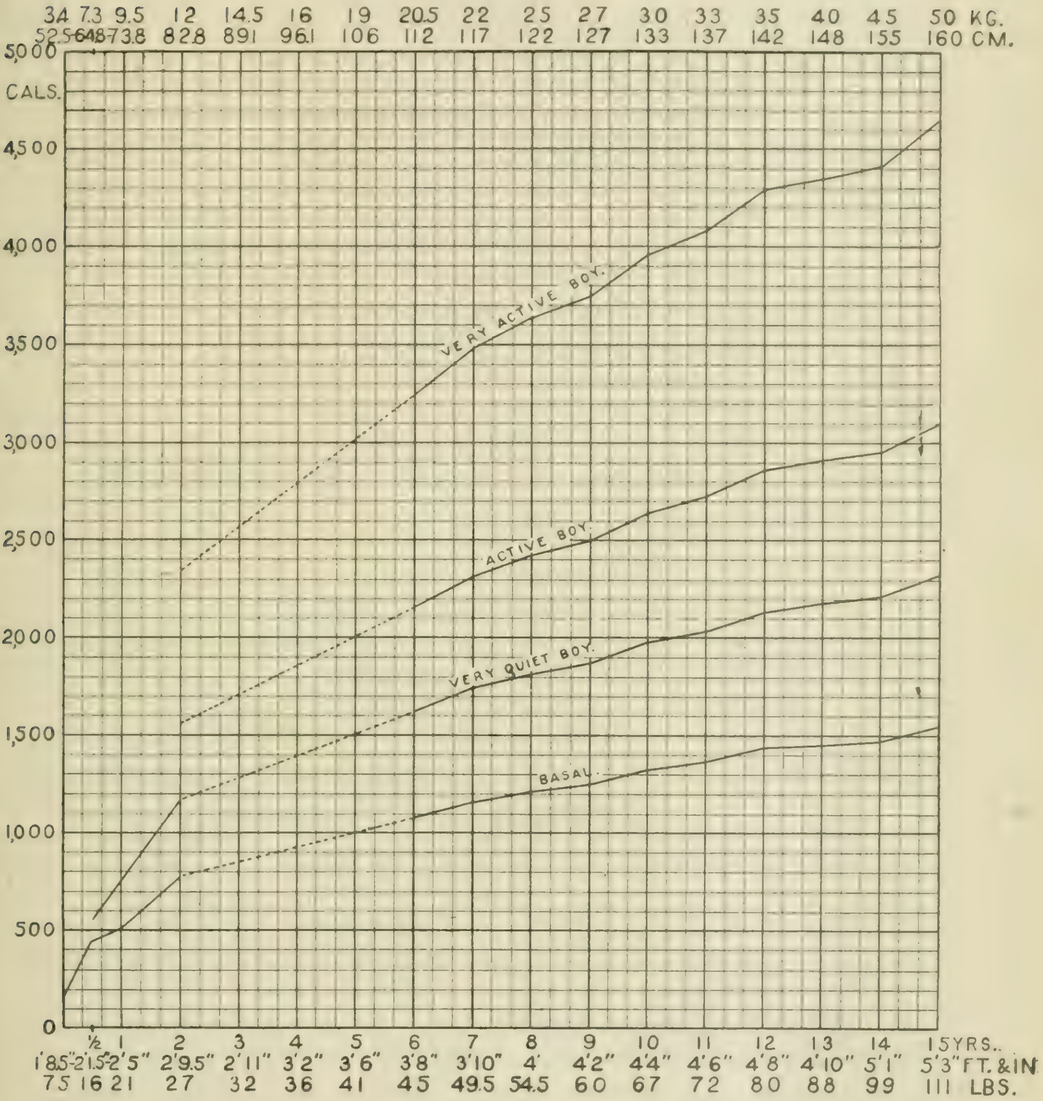
[15] Bailey and Murlin: Am. Jour. Obst., 1915, **71,** 526. Benedict and Talbot: The Physiology of the New-Born Infant. Carnegie Institution of Washington, 1915, Pub. 233.

[16] Murlin, J. R., and Hoobler, B. R.: The Energy Metabolism of Ten Hospital Children Between the Ages of Two Months and One Year. Am. Jour. Dis. Child., February, 1915, p. 81.

[17] Magnus-Levy and Falk: Arch. f. Physiol., 1899-1900, Supplement, p. 368.

[18] Du Bois, E. F.: The Metabolism of Boys 12 and 13 Years Old Compared with the Metabolism at Other Ages. Arch. Int. Med., June, 1916, p. 887.

TABLE 1.—Metabolism in Calories Per Day of Boys from Birth to 15 Years of Age



12 kg., or 26½ pounds; and thereafter rises gradually until at 15 years of age 1,500 calories is needed for a boy of 110 pounds weight.

To this basal requirement must be added something for growth—15 per cent. of the total calories in infancy; and an additional increment for work, etc., whether this takes the form of crying (severe crying increases the basal metabolism 40 per cent. per hour in infancy), or active play, or mechanical labor.

A study by Gephart[19] has shown that boys between 13½ and 16 years of age who actively indulge in athletic sports ingest 5,000 calories daily in their food, or threefold their basal requirement of energy. Whether they really need this or not is another question. Lusk thinks it probable that an active boy produces twice the number of calories measured by his basal metabolism, whereas for one taking little exercise a 50 per cent. additional amount undoubtedly suffices.

The figures given by Lusk are maximal values based on individuals in better than the average nutritive condition. Allen and Du Bois[20] have shown that the basal requirement of energy in men may be largely reduced through emaciation. It appears, however, that a given amount of work is always accomplished at the expense of exactly the same amount of extra calories, no matter what the nutritive condition of the subject. When a man stands upright or sits in a chair, his basal metabolism is increased 10 per cent.

Metabolism of Mother and Fetus.—Murlin,[21] in an address before the Harvey Society of the New York Academy of Medicine, considers in a very broad manner the relation of the mother and her offspring as regards metabolism. He reverts to the conception of August Weissmann:[22] that the germ cells, or reproductive elements are not, strictly speaking, produced by the adult body; the adult body is produced and reproduced by the germ cells as a medium in which the specific stock can be perpetuated. Reproduction is the aim of life. All the cells of the body stand at the service of the germ cells because in them is perpetuated their own being (Hatschek). The ovum is always to a large degree an independent organism capable even in the face of obstacles of looking out for its own nourishment. A certain cell in each follicle is selected to grow at the expense of its fellows because it possesses the complement of enzymes which enable it to appropriate the materials supplied by its less fortunate neighbors. On fertilization this cell receives a fresh impetus. The follicle cells which adhere to it are dissolved away. By the time this is completed the fertilized ovum has normally reached the uterus. Arriving at the uterus, the only reason why a fertilized ovum rather than an unfertilized one becomes attached to the wall is that its cells (for there are many by this time) are hungry and possess the means of satisfying their hunger. The process of implantation is a continuation of the proteolysis by which it lays claim to its nutrient. Wherever the ovum happens to come in contact with the uterine mucosa after the fringe of follicle cells has been digested and absorbed it there adheres and soon dissolves a depression, and finally becomes imbedded, implanted. The mother reacts to protect herself against the invader, or, in modern phrase, to restrict the action of the enzymes. A balance is established, and the two organisms live in mutual tolerance, or as Bar has named it, "harmonious symbiosis."

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[19] Gephart, F. C.: Report of a Dietary Study of St. Paul's School. Boston Med. and Surg. Jour., 1917, **176**, 17.

[20] Allen, F. M., and Du Bois, E. F.: Metabolism and Treatment in Diabetes. Arch. Int. Med., June, 1916, p. 1010.

[21] See footnote 13.

[22] Weissmann, A.: The Germ Plasm, English Translation, London, 1893.

When the placenta is finished the maternal blood is separated from fetal blood by the two-layered trophoderm and by certain mesoblastic structures, making an arrangement practically identical with that of the wall of an intestinal villus. Truly diffusible substances like glucose and urea readily pass the placenta (Morris and earlier workers), probably as readily as they pass the intestinal wall. Glucose arriving at the maternal placenta faster than it can be utilized by the fetus, is stored in the maternal side as glycogen until the last quarter of gestation when the fetal liver begins to assume its carbohydrate function, whereupon glycogen disappears gradually from the maternal placenta. The transfer of fat is still under investigation. Slemmons, in studying the lipoids in maternal and fetal bloods, has reached the conclusion that neither neutral fat nor cholesterol esters pass the placenta at all, but that cholesterol does. Since cholesterol is a colloid in the blood, proof that it passes the placental barrier is tantamount to proof that a selective activity is going on.

How proteins pass the placenta is the most important question of all. Amino-acids can readily find their way through the placenta (Morse). The question is where the indispensable building material is first modified. The weight of evidence is at present more in favor of a vitalistic conception of a placental function than of a mechanistic one.

The transport of iron from mother to fetus cannot be accounted for on mechanistic grounds. It seems certain that the fetus relies for this essential element on destruction in the placenta of the red cells of the mother's blood.

Under the mysterious guidance of the mechanism of heredity the proteins are built up into a new being which reproduces the essential characteristics of the phylum, class, order, genus and species to which the germ cells belong. Experiments lead to the conclusion (Heape-Castle) that a human child is born human not so much because it is nourished by a human being as because the germ cells from which it came are human. It is not yet known just how closely related individual germ cells and the fostering mother must be related in order that development may proceed.

The demands of the fetus on the host for material for growth are very slight. Michel has shown that up to the end of the seventh lunar month not more than one-fourth of prenatal growth in terms of protein and salts has taken place. The total quantity of material needed for development up to the middle of pregnancy could be taken by the mother at a single meal.

That there is a negative nitrogen balance (output of nitrogen derivatives exceeds intake) in the early months of pregnancy is well known. The explanation is to be found in the means employed by the fetus for its nutrition at this stage, proleotytic destruction of the host (uterine mucosa, etc.). Products of proteolysis may well be the cause of "physiological vomiting." This activity is limited with the formation of the placenta and nitrogen retention becomes easier.

There then begins a retention of nitrogen that continues to the end of pregnancy and reaches such proportions that the total retention of nitrogen exceeds the requirements of the fetus, uterus, placenta, membranes and mammaries by a very considerable amount (Höffstrom-Wilson), an amount equivalent to the nitrogen in about 100 liters of milk. Accompanying this and associated with the removal of waste products from the fetus are changes in the urea, ammonia, creatinin, creatin, purin, and undetermined nitrogen, also in the inorganic sulphur, all of which (see many references) are to be explained on physiologic grounds.

A number of observers (Leimdorfer, Novak and Porges, Hesselbach) find a lower alveolar tension of carbon dioxid in pregnant women and state that it appears as early as the first estral cycle followng conception. Losee and Van Slyke confirm this for late pregnancy. It is part of a perfectly automatic respiratory regulation of the hydrogen-ion concentration and protects the host against acidosis.

During the puerperium a great readjustment takes place. Only the nitrogen balance has been studied in women during the involution period, but the same facts probably hold for sulphur, phosphorus, calcium, and magnesium. The chief source for the extra nitrogen found in the urine is the involuting uterus. The output reaches its maximum on the sixth or seventh day. A readjustment of the various nitrogen bodies occurs. There is no acidosis characteristic of the puerperium.

Collateral evidence points to a very great increase in the metabolism of the ovum from fertilization—a seven fold increase in the fertilized urchin egg, rising rapidly to twenty-five fold. The scanty observation available on the developing fetus indicated plainly that the source of energy is carbohydrate, the most readily diffusible of all the foodstuffs. Studies on the new-born have already been reviewed.

Studies on women pregnant with a single fetus show an extra metabolism near term of about 4 per cent. over that of the same woman or other women in complete sexual rest. It is surmised that this is scarcely more than may be accounted for by the increased respiratory activity necessary to preserve the hydrogen-ion concentration of the mother's blood. The total product of conception, added to the mother's body, functions as so much maternal tissue—the high metabolism of the embryo being just counterbalanced by the inactive and relatively inactive structures.

Metabolism of Older Infant.—Talbot[23] points out that a careful review of the literature shows that there have been few instances in which an attempt has been made to obtain the twenty-four hour metabolism of infants. The fundamental experiments of Rubner and Heubner upon three normal infants stand out as giving the only twenty-four hour figures available. On the basis of these and other studies, Heubner maintains that an average normal infant requires per twenty-four hours 100 calories per kilogram of body weight during the first three months of life, 90 calories during the second three months, and 80 or less calories during the last half of the first year of life; and these figures are usually accepted as a basis from which to compute the energy requirements of normal infants.

Talbot utilized normal infants. The plan of observation was to have the infant inside the respiratory chamber as many hours out of the twenty-four as possible so that an accurate measure of the total respiratory exchange could be obtained. The infants were both breast fed and weighed 5.03 and 5.76 kg., respectively. Through intelligent cooperation of those in attendance it proved possible to reduce the time in which the infants were out of the respiratory chamber to one hour and twenty-nine minutes and fifty minutes, respectively.

On making due allowance for the time out of the chamber it was found that the total number of calories used by the infants was 70 and 74 calories per kilogram. What was measured was the actual heat produced by these infants. This represented the energy needs for basal metabolism plus the effect of muscular effort. Energy was of course lost in other ways, such as the potential energy of the urine and feces; this also must be supplied from the food. For the present this loss can only be estimated. Probably the greatest single

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23. Talbot, F. B.: Twenty-Four Hour Metabolism of Two Normal Infants, with Special Reference to Total Energy Requirements of Infants. Am. Jour. Dis. Child., 1917, **14**, 25.

factor to be considered is the fat lost in the feces. This and the urea in the urine should not exceed presumably 15 per cent. of the total measured metabolism in a normal infant. When this has been added the child should remain in equilibrium, neither gaining nor losing. Something must be added for growth. If 20 per cent. is taken for the growth factor, it should give enough leeway for the infant to gain.

These figures, 15 and 20 per cent. added to the former figures, 74 and 70 calories, respectively, make a total food requirement of 100 calories per kilogram of body weight and 94 calories per kilogram of body weight, respectively.

The actual basal metabolism is represented by the total heat produced (74 and 70 calories) less the amount due to muscular activity —15 per cent. of the basal metabolism if the infant is very quiet, 25 per cent. if normally active, 40 per cent. if extremely active. An allowance of as much as 10 per cent. on one side or the other from the average figure of basal metabolism must be allowed for individual variation in infants. A sick baby has a higher "basal" metabolism because of increased restlessness, energy burnt up in fever, or impaired absorption of the food given him, one infant losing 20 per cent. of the food calories in the feces.

The metabolism of boys 12 and 14 years old—clinical calorimetry —has been studied by Olmstead, Barr and Du Bois.[24]

Hunger Phenomena.—The work of Carlson and Ginsberg on hunger contractions in the infant was referred to in this review two years ago.[25] Carlson and Ginsberg introduced a balloon and tube into the stomach of an infant and, using a manometer, secured graphic records of the stomach contractions. To the objection that the presence of the balloon in the stomach acts mechanically to produce gastric contractions, Carlson says definitely that it does not, and gives the following reasons: (1) the presence of the distended balloon in the stomach between the contraction periods does not induce these contractions; (2) in his gastric fistula case the gastric contraction could be observed directly through the fistula without any balloon in the stomach; (3) they come on just as frequently without any balloon in the stomach and produced the same effect (hunger); (4) in pigeons the periodic strong contractions of the empty crop can be seen directly through the skin and a balloon in the crop does not alter their frequency or intensity.

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[24] Olmstead, W. H., Barr, D. P., and Du Bois, E. F.: Metabolism of Boys Twelve and Fourteen Years Old. Clinical Calorimetry. Arch. Int. Med., 1918, **21,** 621.

[25] Holmes, James B.: Recent Advances in Anatomy, Physiology and Pathology of Childhood. Am. Jour. Dis. Child., 1916, **11,** p. 78.

Rood Taylor[26] has utilized a similar apparatus for the study of hunger phenomena in fifty-six infants varying in age from prematurity to 6 months of age, and also in a boy of 2 years with a surgically induced gastric fistula. The paper is a lengthy one. The following findings may be noted:

Confirmation of previous work that hunger contractions are greater in the new-born infant, and determination of still greater hunger contractions in the stomachs of prematurely born infants. Inhibition from the mouth is psychic in character and does not occur in young infants. Reflex inhibition from the presence of food in the stomach is present in infants of all ages; it may be only partially developed in young infants. In normally developing breast fed infants, hunger is not ordinarily an immediate cause for crying. In infants that are not well fed hunger contractions may occur before the stomach has been emptied, and consequently their presence is not in itself evidence that the stomach is ready for food. Hunger contractions may be present when the temperature (rectal) ranges between 104 and 105 F.

Taylor[27] has investigated also the appetite secretion of gastric juice in the infant. "There is apparently a gastric element in appetite. The contractions of the stomach institute hunger. Its profuse and rich secretion causes an entirely different sensation—not painful, but pleasant. This directs the flow of consciousness toward the matter of taking food." Much has been written regarding the presence or absence of this appetite or psychic secretion of gastric juice in the young infant. Taylor described an apparatus by which sham feeding can be carried out and gastric juice collected under conditions which give positive evidence of the amount secreted. He finds there is no appetite or psychic secretion of gastric juice in the young infant. Also that the empty stomach of the hungry infant secretes a gastric juice which is often as acid as that found in the adult's stomach—the more profuse the secretion the higher its acidity. He says that the secretion is not neutralized in the stomach, but flows out into the small intestine. Regurgitation through the infant's pylorus does not occur.

Allaria[28] points out that there are certain chemical and mechanical advantages of having the milk well mixed with saliva and estimates that the infant secretes an amount equal to from 10 to 20 per cent. of the ingested food. The tube fed infant may do without this in part, but there is no evidence that the gastric secretion is less than that of the actively nursing infant. "Therapeutic starvation in acute

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26. Taylor, Rood: Hunger in the Infant. Am. Jour. Dis. Child., 1917, **14,** 233.

27. Taylor, Rood: Hunger and Appetite Secretion of Gastric Juice in Infants' Stomachs. Am. Jour. Dis. Child., 1917, **14,** 258.

28. Allaria, G. B.: Jahrb. f. Kinderh., 1911, **74,** 252; ibid., Pediatria, 1911, **19,** 10. Cited by Taylor.

alimentary disorders and in summer diarrhea may owe its success in part to the heightened tonus of the alimentary tract, and in part to the pouring out of a highly acid detoxicating and disinfecting gastric juice into the small intestine."

Gerstley and Hoskins[29] have studied the effect of hunger on "nervous irritability" in dogs, as shown by the changes in the electrical excitability. Zybell in his clinical studies on spasmophilia concluded that any prolonged hunger aggravated the condition. Gerstley and Hoskins say that they carried out their examinations in the manner ordinarily employed in obtaining the reactions in children and that they found difficulty in obtaining any sort of definite standard. "In a normal dog, even at best, the reactions show extreme variability, changing not only from day to day but sometimes almost minute by minute." Other technical difficulties obtained. They failed to show any constant parallelism between the length of hunger and the degree of electrical irritability.

Malnutrition.—In a report by the Public Health Committee of the New York Academy of Medicine[30] malnutrition is defined as distinctly a pathologic entity, not a disease but a morbid physical condition. It may be symptomatic of disease or it may be the only evidence or result of defective metabolism or of complex and divers physiologic and environmental conditions. Whether caused by unsanitary surroundings, improper habits of life, lack of sleep and unsuitable food, or by poverty and disease, malnutrition is a social menace, as it hampers the natural development of functions of mind and body and predisposes its victims to a permanent life handicap. Every effort should be made to control it among children; its prevention is a distinct public health function.

Examination of New York school children has shown a yearly increasing per cent. of malnourished children. About 16 per cent. of the children are reported to need either supervision or medical treatment. Both the health department and the Association for Improving the Condition of the Poor consider 10 per cent. of the total number of school children an underestimation of the extent of malnourishment. In Philadelphia it was found in one section that 8 per cent. of the children came to school with no breakfast and 60 per cent. with what was considered an insufficient breakfast. It is clear that the problem is a great one.

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[29] Gerstley, Jesse R., and Hoskins, R. G.: A Study of the Effect of Hunger on Nervous Irritability. Am. Jour. Dis. Child., 1917, **15**, 336.

[30] Report of Public Health Committee of New York Academy of Medicine. Malnutrition Among Schoolchildren. Med. Rec., New York, 1918, **93**, 311.

In public discussions of malnutrition *poverty* is usually assigned the first place as a cause. Yet "however plausible the connection between low economic status and undernourishment may be, scientifically established proof is lacking of the causal relation between the two." Families having the same income and the same number of children vary greatly in their nutritional state. Ignorance and bad domestic management are potent factors. An English investigator found the causes in order of importance to be (1) influence and reaction of disease; (2) strong evidence of neglect, dirt or drink, and (3) defective feeding due to ignorance or poverty. Three per cent. of the children owed their condition to being pampered. The factor of housing cannot be dissociated from the accompanying conditions. These may all be called extrinsic causes.

Intrinsic causes include such debilitating factors as chronic absorption from diseased tonsils, decayed teeth, or obstructed nasal breathing, things that can be remedied, as can also some of the respiratory or digestive disturbances. The agencies that are available for combating the conditions are:

(*a*) Clinics for malnourished children—(see report of one as given later).

(*b*) Fresh air classes—maintained primarily to combat tuberculosis; providing of meals given up because of the high cost and discovery that many patients neglected to provide children with breakfast when meal would be given at school.

(*c*) Tuberculosis preventatorium—where children of tuberculous diatheses are kept six months and given medical, educational, and institutional care of high order.

(*d*) School lunches—dealt with more fully later.

(*e*) Baby welfare stations—demonstrations of cooking cereal, and how best to expend a dollar for cereals; practical instruction in other cooking.

(*f*) Diet kitchen—opened in connection with settlement houses and the like.

(*g*) Fresh air funds—providing camps; need of better supervision of rest and diet, and need of longer stay for many children.

(*h*) Education—in some sections more necessary among native born parents than among foreign born (Mauny).

School Lunches.—A considerable part of the report is devoted to a consideration of the "school lunch." The practice of feeding children at school, we are told, is not a new venture in the educational world. It has been known in Germany since the end of the eighteenth century, and it was introduced in France in 1849, and in England in 1866. The difficulty of instructing children who suffer from malnutrition has been recognized by schoolmasters, and arrangements have been made to provide gratuitous meals at school, paid for from the public funds. In America the practice has been different in that it is recognized that many children, even those of the very poor, bring several coppers with them to spend during recess, usually for candy and indigestible articles. These same pennies can buy wholesome and nutritious food at the school, if the same is properly organized.

Indigent children may receive meal tickets from the teachers, the cost being covered by a special fund.

The experience of Philadelphia is reviewed at some length. A five years' experience fully established the fact that "children will buy wholesome food at school if given the opportunity," and that the service can be put on an almost self-supporting basis. It was found that 66 per cent. of the expense was for food, 32 per cent. for supervision and wages, and 2 per cent. for repairs and replacing of equipment. In New York where lunch service is maintained in thirty-five elementary schools, it is found that about one-fifth of the children avail themselves of the lunches. The money paid by them covers only the cost of the food.

The food served to the children is examined as to quality and prepared under carefully supervised sanitary conditions. The menus are prepared by a trained dietitian; they must not offend religious or racial prejudices, nor fall below a desired standard of food value; the proper balance of constituents must be maintained. The children are free to select the foods, but all must buy a bowl of soup before anything else can be obtained.

In Table 2 are shown some of the combinations of food that the children were able to purchase several years ago at a cost of three cents. The same combinations now cost six cents.

TABLE 2.—Food Combinations for School Lunches

	Calories Per Portion		Calories Per Portion
Green pea soup	128.31	Vegetable soup	85.00
Bread, 2 slices	200.00	Egg sandwich	236.00
Apple sauce	108.57	Rice pudding	108.76
	436.88		429.76
Cream of barley	120.47	Clam chowder	82.00
Cheese sandwich	250.17	Butter sandwich	247.25
Chocolate pudding	101.50	Jelly tarts	83.85
	472.14		413.10
Macaroni and tomato	105.29	Bean soup	111.27
Apple jelly sandwich	240.17	Bread, 2 slices	200.00
Cocoa	100.00	Prunes	180.00
	445.46		491.27

The committee makes numerous recommendations directed chiefly toward dissemination of knowledge of proper nutrition and practical cooking, and improvement of children's lunches and the conditions under which they are eaten. They recommend that school lunches be extended. If private means were not available to assume the desired extension, it should be taken over by the municipality.

Classes for Undernourished.—Smith[31] reports his experience with a class of 188 undernourished children drawn from the poorest class of dispensary patients (New York City). No child was admitted to the class unless he was 5 pounds or more under weight for his age. The children returned at intervals of one week to a month. At least one visit was made to each home, and the cases were followed up as far as one social worker could do this. Some adult member of the family was required to come with the child for the first few visits.

A fairly complete history was made on admission to the class, with particular attention to those facts that bear most directly on malnutrition. The social worker checked up the data and added other facts. The general plan was to make a careful diagnosis, to correct remediable physical defects, to determine and correct any economic factors that had a bearing on the case, and to try to improve the diet and hygiene of the child by every possible means.

The child's daily life was gone over with the attendant. If decayed teeth were present the child was referred to or taken to a dentist. If tonsils or adenoids were giving symptoms (or if they were much enlarged) operation was advised, provided the child's general condition warranted it.

A printed diet list was provided. The first lists used were simply ideal diets for a child, but it was found the expensive foods occupied the most prominent place in the lists. The lists were then rewritten several times, until finally a somewhat unique form was adopted. This contains six columns. In the first three are indicated (1) the meal and the dishes stated in general terms; (2) the quantities of each dish; (3) simple directions for cooking. In the next three columns are indicated (1) the cheaper article of food that may form the dishes, (2) the more expensive, (3) the most expensive. Expensive is here used to mean low nutritive value in proportion to price paid—for example, corn flakes, puffed rice, etc. Rules for eating are attached. Also a list of forbidden articles.

A food exhibit was provided. It was based on the day's total ration. Three meals were laid out each day, and each consisted of suitable dishes in proper amount. The visual impression made on the mother and child was found to add tremendously to the significance of the printed list of foods in the diet list. The imitations were so real that nearly everyone was deceived at first glance.

Class talks were given frequently. Weekly return visits were sought. A photograph of each child was attached to the history. They aroused the interest of the children in the class and later ones were useful in showing improvement. They were made inexpensively by lining up several children for one exposure with a cheap camera and then cutting up the finished print.

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[31] Smith, Charles Hendee: Methods Used in a Class for Undernourished Children. Am. Jour. Dis. Child., 1918, **15,** 373.

By use of these methods it was found possible, even among the poorest class of dispensary patients, to make 57 per cent. of the children gain at 1.7 times the average rate for their ages, and 22 per cent. at about the average rate. In the remaining 21 per cent. there was in every case one or more easily ascertainable reasons for the failure—among the significant facts were: low family income (?); failure of mother ever to attend class, a markedly positive von Pirquet reaction, inability of mother to speak English. "It seems fair to conclude that the class method is of value in the treatment of undernourished children even when they must be handled in large numbers."

Rations for boys' military training camps has been made a subject of study by Fitch.[32]

Miscellaneous.—Hess and Unger[33] have investigated the diet of negro mothers in New York City. They selected a district with a population of about 9,000, composed almost entirely of negroes. It was found that the diet as a rule afforded ample calories, but that it was not well balanced. There was an excess in the intake of protein (beef, cooked very frequently as stew), adequate carbohydrate, and a deficiency of about 25 per cent. of the fat in the dietary. There was a preponderance of canned and dried vegetables, fresh vegetables being taken on the average but once a week, and fresh fruit about twice a week. The dietaries were thus deficient in fat and in calcium and other salts, for which we depend largely upon milk, vegetables and fruits. Since the majority of the negroes came from the West Indies, St. Kitts, the Barbadoes, and St. Croix, where they were accustomed to a diet consisting mainly of fresh vegetables and fruits and where rickets is practically unknown, Hess and Unger argue that the change to a deficient dietary in the mothers may be largely causative of the striking amount of rickets in their offspring.

Chapin[34] calls attention again to the heavy morbidity and mortality that exist among neglected and abandoned infants. There are but two plans for handling these children: they can either be boarded out or collected in institutions. After reviewing the results obtained by representative institutions and contrasting their work with the figures obtainable where babies are boarded out and properly supervised, Chapin concluded that the home, though poor and imperfect, is better in the long run for the little child than the institution.

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[32] Fitch, W. E.: Rations for Boys' Military Training Camps. Military Surgeon, 1917, **40,** 518.

[33] Hess, A. F., and Unger, L. J.: Diet of the Negro Mother in New York City. Jour. Am. Med. Assn., 1918, **70,** 900.

[34] Chapin, Henry Dwight: Systematized Boarding Out vs. Institutional Care of Infants and Young Children. New York Med. Jour., 1917, **105,** 1009.

Two factors militate in favor of a high death rate in institutions: (1) lack of individual care, and (2) lack of fresh air. Cross infections from ordinary colds, influenzas and respiratory diseases are always liable to be dangerous where many individuals are crowded together; epidemics are frequent. The child contracts disease because it is in an institution.

By boarding out the danger of spreading communicable diseases are reduced to a minimum. By no other known method of handling can so many children of this type be cared for with so little spread of infection (data from the Speedwell Society, Morristown, N. J.). Children in a boarding home if they do not succumb to actual disease are usually as strong as other children in the family; infants who are retained very long in institutions are not apt to be vigorous. Chapin says:

> Boarding, if properly employed, will not only give better results, but is cheaper in operation. To the money locked up in the original cost of the plant must be added the cost of operation and the amount of taxes remitted; all this enters into the real expense of the work done by them. In boarding out, the money goes into aiding the upkeep of normal homes. The constant oversight of doctor and nurse helps each foster mother in the care of her own children. The general standard of living may also be raised.

Bateman,[35] writing from the Sheffield Laboratory of Physiological Chemistry (Yale University), points out that evidence has been accumulating during the past fifteen years which shows that raw egg-white occupies an exceptional position among native foodstuffs. He reviews this evidence. It is shown that native egg-white offers serious obstacles to digestion. This is an important matter, for raw eggs and egg-white (egg albumin) have enjoyed a great vogue as the mainstay of various diets, especially for the sick. Certain recent writings have served to support this use, but Bateman shows that they rest on mistaken assumptions. He feels that his study shows that the current reasons for using raw egg-white are not well suppported, and indicates that use of raw egg-white is decidedly inadvisable. "A substance which fails to stimulate a flow of gastric juice and is antipeptic, which hurries from the stomach, calls forth no flow of bile, and strongly resists the action of trypsin, which is poorly utilized and may cause diarrhea has evidently little to recommend it as a foodstuff of preference for the sound person, let alone for the invalid."

Raw egg can be made digestible by heating it at 70 F., by incubation with dilute acids and alkalis at 37 C., by precipitation with alcohol, chloroform, or ether; by partial digestion with pepsin, and by conversion into alkali metaprotein.

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[35] Bateman, W. G.: The Use of Raw Egg in Practical Dietetics. Am. Jour. Med. Sc., 1917, **63,** 841.

Lack of space forbids more than a passing reference to the studies on the digestibility of the so-called war-breads,[36] Victory bread, etc.

Pease and Rose[37] have carefully studied the banana from a nutritional point of view. This fruit has been regarded as of doubtful value in the dietary of children. Its chief food constituents are the carbohydrates, which amount to about 22 per cent. In the green fruit these are in the form of a starch, but as the fruit ripens this is converted into, first, sucrose and finally into invert sugar. The protein content (less than 1 per cent.) is of unknown nature; the fat and fiber are negligible. The ash is important, being similar to that of other common fruits. Vitamins are doubtless present in fair share. When fully ripe, banana is apparently a good fruit for children, provided it does not crowd out other foods more essential for growth. It may for a time replace cereals and potatoes, in part. The *underripe uncooked* fruit should never be given to children.

The banana is fully ripe when the peel takes on a golden yellow and begins to be speckled with brown. It finally becomes brown all over and is then still edible provided the cover is still intact and the pulp shows no signs of fermentation. (The brown color of ripening must not be confused with the brown patches due to bruising.)

An adult receiving a diet of 1,000 gm. banana, 1 quart of milk and 1 cup of sweetened coffee daily for a week experienced comfort, satisfaction and unimpaired efficiency. The utilization of the banana carbohydrates in this and similar cases was 98.8 per cent. In the experiments on children the banana was introduced as a substitute for the more starchy foods such as cereals and potato, and ranged in amount from one small banana to three-quarters of the day's carbohydrate quota. They were mashed to prevent bolting an unmasticated lump. The stools were examined for signs of fermentation and analyzed for the presence of starch and dextrins.

The nutritive value of the banana is relatively high, approximately 1 calorie per gram of pulp; and its carbohydrates appear to be not less assimilable than those of cereals and potatoes. In the raw fruit the digestibility is directly proportional to the ripeness of the fruit—conversion of starch to sugars. There is no positive evidence that the banana influences bowel movements. Prolonged use of the underripe fruit produced undesirable symptoms. Baked bananas both from the green and early yellow stage were well utilized.

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[36] Spriggs, E. I., and Weir, A. B.: Digestibility of Bread Made from Two Parts of Wheat and One Part of Oats, Barley, Maize, or Rice. Lancet, London, 1917, **2**, 724 (for example).

[37] Pease, Marshall, and Rose, Anton R.: The Banana as a Food for Children. Am. Jour. Dis. Child., 1917, **14**, 379.

Meyers and Rose found that larger amounts of the sugars could be given in the form of bananas than as pure sugars without causing digestive disturbances. From a number of observations it seemed that the banana was a specially valuable form of food in the dietetic treatment of cases of nephritis with nitrogen retention. As the ash is alkaline, it might have some value in combating a tendency to acidosis.

Bosworth, Bowditch and Giblin,[38] working in a school where it is customary to feed topmilk formulas, state that it is well recognized that the digestion and absorption or nonabsorption of fats is probably a source of the greater part of the trouble in feeding cow's milk modifications. This difficulty they believe lies not so much in the fat itself as in the accompanying inorganic constituents of cow's milk dilutions. Cow's milk is especially rich in calcium and phosphoric acid, substances which the young of the cow use to develop rapidly growing bone tissue, but which the infant uses very sparingly. The excess is eliminated by the infant in the feces as insoluble calcium phosphate and calcium soaps. While this mode of eliminating the excess calcium present in the cow's milk is in one way a protection to the infant, in that it prevents the calcium from entering the body fluids and tissue in organic combination, subsequently to set up a toxic condition (unpublished work from their laboratory) it may, on the other hand, bring about marked nutritional disturbances.

The examination of many stools from bottle-fed infants has led them to believe that although neutral fat, free fatty acids and soaps may all be found in these stools, the appearance of neutral fat and fatty acids, except in the case of diarrhea, are wholly secondary, being due to a faulty feeding which allows an excessive amount of calcium, available for soap formation, to enter the intestines. There the conditions are very favorable for the formation of insoluble calcium salts, which, as they are precipitated, may carry down with them by occlusion both neutral fat and free fatty acid. Data submitted are to show that the soaps present in the stools of bottle-fed infants receiving modified milk (containing 2 to 3 per cent. fat) are almost wholly insoluble soaps, and, as calcium is the only insoluble base present in appreciable amount, it is concluded that the insoluble soaps are calcium soaps.

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38. Bosworth, A. W., Bowditch, H. I., and Giblin, Louise A. (Boston): Studies of Infant Feeding. X. The Digestion and Absorption of Fats. 1. Calcium in Its Relation to the Absorption of Fatty Acids. AM. JOUR. DIS. CHILD., 1918, **15**, 397.

In order that the soaps formed from the fatty acids which are produced by the digestion of fats may be assimilated, it is necessary that they be absorbed and pass through the intestinal wall into the body fluids. To be thus absorbed they must be soluble in the intestinal juices, or more definitely speaking, in the bile. A study of the solubility of calcium soaps in bile, while not yet complete and rather inconclusive, is thought to indicate that calcium oleate shows a higher degree of solubility in bile at 37 C. than do the calcium soaps of stearic, palmitic or myristic acids. This, if true, would explain the preponderance of the calcium soap of palmitic acid over other soaps present in infants' stools.

The influence of the kind of calcium salts present in the food on the amount of calcium soaps eliminated from the stools was studied by feeding synthetic (calcium free) food to which various salts of calcium were added (dicalcium phosphate, calcium caseinate, and calcium caseinate and acetate). In this connection it is pointed out that it is not the mere presence of calcium salts in the food which determines the presence of calcium soap in the stool, for other factors enter in, such as the forms in which the calcium is present in the food, bacterial activity within the intestines, and the amount of hydrochloric acid secreted into the stomach, since this may change the forms of calcium compounds.

Having been led by their investigations to believe that many of the troubles encountered with bottle-fed infants receiving cow's milk must be attributed to the ill effects produced by the calcium in cow's milk, Bosworth, Bowditch and Giblin have perfected a method for "reconstructing" cow's milk which permits them to remove nearly all the calcium from the original milk. Inorganic phosphorus and calcium are then added in desired amounts. In other words, not only are the percentage of protein, fat, and sugar varied as needed, but an attempt is made also to properly balance the mineral elements of the food.

This work is in line with the tendency to pay increasing attention to the mineral elements of food.

Hess and Unger[33] present work to show that so far as the colored race is concerned, the development of rachitis is based on some dietetic insufficiency which appears to be satisfied by the administration of cod liver oil. Because rickets is a predisposing cause of respiratory diseases, such as pneumonia, bronchitis and possibly whooping cough and tuberculosis, the successful prevention of rachitis among infants would tend to reduce infant mortality.

The fact that breast fed children fall victims to this deficiency disease suggests that probably the dietary of the mother lacks a certain required protective substance, as for example, is the case among mothers in the Philippines, where children develop beriberi. Cow's milk in itself does not always seem to supply the deficiency; and inferior grades of condensed milk and proprietary infant foods more frequently fail.

Hess and Unger think it possible that cod liver oil may prove as prophylactic against rickets as orange juice is against scurvy. If so, it should be supplied at cost in baby stations and its use taught generally.

Hess[39] holds that a faulty diet is only one of the several factors in the pathogenesis of infantile scurvy. In a recent study (1917) it has appeared to him that pasteurized milk is a contributory cause if it is not fresh—i. e., if given twenty-four to forty-eight hours after pasteurization. From this point of view milk pasteurized in the city is preferable to milk pasteurized at the creamery, which reaches the consumer much longer after the heating process. Ageing seemed to have a greater rôle in the production of scurvy than heating, whether the milk was pasteurized or raised to the boiling point. It was found (Hess) that even raw milk on ageing loses its antiscorbutic properties. However, infantile scurvy is not, he believes, a simple dietary disease, but rather one due to faults in the diet allowing the intestinal bacteria to elaborate toxins; that is, an intestinal intoxication or an auto-intoxication due to the overgrowth of harmful bacteria, the product of an unbalanced flora, which is no longer controlled by a proper dietary. As the toxin may not always be the same, the question is raised whether from a strictly etiologic standpoint the disorder should be regarded as an entity.

Oliguria is a common symptom of scurvy. Hess thinks the mild therapeutic effect of citric acid may be ascribed partly to its diuretic properties. Orange juice is found also to bring about marked diuresis.

Some hemorrhages that occur are to be regarded as scorbutic; others are due possibly to the susceptibility to infection (furunculosis, nasal diphtheria, "grippe," etc.) that is an important and striking symptom of scurvy (Hess), and are to be regarded rather as focal complications.

When scurvy is latent among a number of infants and an infectious disease (such as "grippe") is suggested, scurvy may appear in epidemic form.

Torrey and Hess[40] revert to the question that has been raised as

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39. Hess, Alfred F.: Infantile Scurvy. V. A Study of Its Pathogenesis. Am. Jour. Dis. Child., 1917, **14,** 337.

40. Torrey, J. C., and Hess, A. F.: The Relation of the Intestinal Flora to the Scurvy of Guinea-Pigs and of Infants. Proc. Soc. Exper. Biol. and Med., 1918, **15,** 74.

to whether scurvy in guinea-pigs and in human beings is due to constipation and to the putrefactive activity of the bacteria in the intestinal tract. They studied the intestinal flora of guinea-pigs on diet that led to the development of scurvy, and diets containing antiscorbutic properties that cured the same. They found no change in flora on adding orange juice to the diet. It seemed that the development of scurvy was not associated with an overgrowth of putrefactive bacteria. (The actual amount of putrefaction present, however, can only be determined by a chemical study, and this was not made.)

Holt, Courtney, and Fales[41] report on the effect of administering cod liver oil to an 8½ year old girl who weighed but 29 pounds, and was of the height of an average child of 3 years. A tentative diagnosis of infantilism of intestinal origin had been made. There were but slight evidences of old rickets and none whatever of active rickets. During ten months of improved digestion (from the omission of certain disturbing articles of food) and an enlarged diet, particularly the addition of milk, cod liver oil, and a preparation of malt in which it was administered, the child grew 2 inches in height and gained 9½ pounds in weight.

The cod liver oil was administered with the hope that it might influence salt retention. At the same time, by increasing the diet, especially the amount of milk, an attempt was made to increase the salt intake. Careful metabolic studies were made. The most striking changes that occurred under the treatment were in the salt balances. Instead of negative balance in total ash of 6.77 per cent., a positive balance of 14.3 per cent. is shown. All the salts showed positive balances. The most marked change was in the calcium.

The results in this case, which far exceeded the expectations, are thought to show conclusively how essential to proper growth is assimilation of the salts ingested. In this instance the most important factor is thought to have been the cod liver oil, the next being the milk.

Phosphorus.—Phemister[42] contributes an article on the effect of phosphorus on growing normal and diseased bones. Since the experimental work of Wegner[43] phosphorus has been used more or less extensively as a therapeutic agent in disorders of ossification. Wegner administered ¹⁄₄₀₀ grain of yellow phosphorus daily to young growing dogs, cats and chickens over considerable periods of time and observed definite changes in the bones, both in the diaphysis and epiphysis.

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[41] Holt, L. E., Courtney, A. M., and Fales, H. L.: Effect of Cod Liver Oil on Growth in Case of Intestinal Infantilism. Am. Jour. Dis. Child., 1917, **14,** 222.

[42] Phemister, D. B.: The Effect of Phosphorus on Growing, Normal and Diseased Bones. Jour. Am. Med. Assn., 1918, **70,** 1737.

[43] Wegner: Virchows Arch. f. path. Anat., 1872, **55,** 9.

Adult bones were not affected. In fractures the formation and ossification of callous was stimulated. Kassowitz[44] repeated and confirmed Wegner's experiments and brought out the additional fact that from two to four times the dose of phosphorus that produces osteosclerosis, leads to osteoporosis. Kissell's[45] negative results were perhaps thus to be explained. Miwa and Stoeltzner[46] were able to confirm Wegner's findings in a few of their experiments, and Stoeltzner, as a result of extensive clinical experience, became a firm advocate of phosphorus therapy in rickets.

The effect of administering cod liver oil and phosphorus in increasing the calcium and phosphorus retention in rickets has been known for some years. Schabad[47] has maintained that phosphorus when administered alone in the usual therapeutic doses causes no increase in calcium accumulation in the body, and in some cases studied even accelerated its elimination. Cod liver oil caused a moderate increase, while cod liver oil and phosphorus caused a marked increase in calcium accumulation. Cod liver oil is apparently not, as some have thought, merely a convenient vehicle for phosphorus. Lime salts, especially calcium lactate, when given with cod liver oil and phosphorus, increase still further the calcium accumulation. Schabad concludes that the cod liver oil, not the phosphorus, is the primary active substance, and that the phosphorus acts secondarily by augmenting the accumulation that is started by the oil. (Schloss[48] questions the value of phosphorus in the combination; then in a later communication states that calcium phosphorus preparations alone, when given with breast feeding, are almost as effective in improving the calcium and phosphorus balances as when they are used with cod liver oil. He concludes that the nature of the food and the condition of absorption in the body are of more importance than the form of salt addition.)

Phemister points out that as 98 per cent. of the calcium of the body is stored up in the bones, they should show a variation in calcium content in case of an increase or decrease in the amount retained in the body; that this can be determined either by studies at necropsy or by roentgen studies of the bones of the living; that no evidence of either kind is offered by Schabad or Schloss in support of their claims. Hence the interest of his paper, which is fully illustrated with roentgenograms. His findings indicate that phosphorus (here given alone, and continued in one instance as long as eight months) affects the bones of normal children in much the same way as described by Wegner for experimental animals. The effect on enchondral bone is especially well marked. Also there is for some time after the phosphorus is stopped a continued but less well marked overproduction of bone in the juxta-epiphyseal region of the shaft that is probably due either to the cumulative effect of the phosphorus or to the stimulating influence of the excessive stores of calcium salts in the neighboring bone.

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[44] Kassowitz: Ztschr. f. klin. Med., 1884, **7.**

[45] Kissell: Virchows Arch. f. path. Anat., 1896, **144.**

[46] Miwa and Stoeltzner: Jahrb. f. kinderh., 1898, **57.**

[47] Schabad: Ztschr. f. klin. Med., 1909, **57,** 454; 1909, **58,** 94; 1910, **59,** 435; Jahrb. f. Kinderh., 1910, **72,** 1.

[48] Schloss, Ernst: Jahrb. f. Kinderh., 1913, **28,** 694 (cit. from Holt).

Judging from the general effect it produces, phosphorus if given early in fractures during the active period of repair should stimulate callous formation and ossification. "In nonunion, however, when the natural reparative impulses have been exhausted, little should be expected from its use." In rickets, during the florid stage, "the bony tissues have lost the power of depositing lime salts, and as phosphorus is presumably unable to restore the power, no appreciable effect from its administration would be detectable by means of the roentgen ray, although it may increase the amount of osteoid tissue formed."

Studies like the above labor under the difficulty of getting plates that in exposure, development, etc., are really comparable. Phemister's work is of interest in showing that phosphorus when given alone may have a marked stimulating effect on bone production in the zones of normal growth, and in contradicting the views of Schabad relative to calcium metabolism in healthy children.

Dicalcium Phosphate.—Bowditch and Bosworth[49] have carried out studies to show whether the dicalcium phosphate ($CaHPO_4$), which is present in cow's milk to the extent of 0.175 per cent., is available as food. They conclude that it is not available to children under 4 months of age and only partly available to older children. They hold that the utilization of calcium phosphate by the older children is probably dependent on the more abundant secretion of hydrochloric acid. In calculating the amount of mineral elements present in modified cow's milk for use in infant feeding, they would consider the dicalcium phosphate as unavailable and make a corresponding reduction from the total mineral elements in milk. It is possible to render the urine phosphorus-free by feeding sufficient soluble calcium to precipitate the phosphorus of the food as insoluble calcium phosphate.

"Vitamin."—McCollum and Simmonds[50] say that it has become evident that among the thousand or more chemical substances which occur in animal and plant tissues it is essential only that the diet of the mam-

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[49] 49. Bowditch, H. I., and Bosworth, A. W.: Availability of Dicalcium Phosphate When Present as a Constituent of Infant's Food. Boston Med. and Surg. Jour., 1917, **177,** 864.

[50] 50. McCollum, E. V., and Simmonds, N.: The Nursing Mother as Factor of Safety in the Nutrition of the Young. Am. Jour. Physiol., 1918, **46,** 275.

mal shall contain the following: Sixteen or seventeen amino-acids which result from the digestion of the complete proteins; the carbohydrate glucose or one of its polysaccharids (starch, dextrin, etc., or other sugar which in the body is convertible into glucose); probably nine inorganic elements in the form of suitable compounds (Ca; Mg; Na, K, Cl, P., I. Fe, S), and two as yet chemically unidentified dietary essentials, fat-soluble A, and water-soluble B.

Lack of certain of these substances leads to disease (beriberi, for example, or (Funk) scurvy and pellagra), or apparent mere lack of growth. This may be studied in animals.

Young animals, for example, cannot grow when fed a single seed or a mixture of seeds even though the latter be supplemented with purified protein and a fat containing fat-soluble A. The inorganic factor is the first limiting factor, and sodium, chlorin and calcium must be added before growth becomes possible.

The extent to which the maternal organism through the secretion of the mammary gland can serve as a factor of safety for the suckling is still very little understood. Examples of the exercise of a synthetic function by the mammary tissue are seen. There is evidence also of variability of the milk depending on the composition of the mother's food. Indeed, the quality of the milk as judged by its growth producing power is dependent in a surprising degree on the quality of the diet of the mother. McCollum and Simmonds' studies on rats confirm and explain Andrew's[51] studies on human milk, "and establish the fact that milk production may take place under dietary conditions such that the product is deficient in certain complexes necessary for growth."

The nursing mother, then, does act as "a very important factor for her young in that her mammary tissues can remove from the blood all elements necessary for the production of milk, approximately more nearly the normal in quality than was the food from which it was produced."

Fischer[52] writes in a nontechnical manner on the subject of vitamins and recent literature pertaining to their application in infant feeding.

Roper and Eddy[53] in presenting a study of the use of "pancreatic vitamin" in cases of marasmus refer to Casimir Funk's isolation of "vitamin" from rice polishings, in 1911, and later from yeast and other sources; Mendel and Osborne's recognition of certain substances found in butter fat as necessary for growing rats, and McCollum's grouping of the two as (1) fat-soluble A (his name for Mendel's butter fat factor), and (2) water-soluble B (his name for Funk's "vitamin"). McCollum has suggested that the name vitamin be dropped altogether.

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[51] Andrews (Philippine Jour. Sc., Series B, 1912, **7,** 67) induced Philippine women whose infants had just died of beriberi, to nurse young puppies. These in all cases developed paralysis of the posterior extremities, which is one of the characteristic symptoms of the disease.

[52] Fischer, L.: Recent Literature Pertaining to Vitamins: Their Application in Infant Feeding. Med. Rec., New York, 1917, **92,** 13.

[53] Roper, J. C., and Eddy, W. H.: Use of Pancreatic Vitamin in Cases of Marasmus. AM. JOUR. DIS. CHILD., 1917, **14,** 189.

All attempts to purify or isolate these substances further have failed. Any chemical test for their presence is lacking. According to Roper and Eddy we have at present only two ways of determing their presence in a given diet or substance, namely, by producing polyneuritic conditions in pigeons through feeding of polished rice and then treating the birds with the "vitamin"-containing substance, or by feeding rats on a maintenance diet and then by the addition of the vitamin to the diet noting the improved tendency of the growth curve as a result. The agent or substance that prevents polyneuritis may not be the same as that which prevents growth. Orange juice, for example, which contains something that prevents scurvy, does not promote growth.

Seidell having shown that the active substances can be obtained from their crude solutions without loss of strength through shaking them with a special form of fuller's earth, Lloyd's reagent, which has the power of absorbing them, Eddy and Roper utilized Lloyd's reagent to prepare a powder from an acid alcoholic extract of minced lambs' pancreas, such that 1 gm. of the powder contained "the vitamin of 54 gm. of pancreas." The efficiency of the preparation in growth stimulation was demonstrated in white rats. They administered it to ten infants, six of which were cases of marasmus. Observations on a typical marasmic infant seemed to show that the preparation had a definite growth-producing effect. Control studies on rats showed the cereal and condensed milk diet which the infant was receiving was markedly lacking in natural vitamins, and that the addition of pancreatic vitamin to such a diet was sufficient to convert it into an efficient growth-producing diet. Five other infants offered further evidence for the same conclusions. In all five cases the infants gave every indication of marked improvement physically. In three other infants suffering from malnutrition, growth had already begun when the extract was added to the diet, and the effect was not so clearly demonstrable.

Eddy and Roper think the use of "pancreatic vitamin" seems to offer definite hope of success as an agent for stimulating the growth of marasmic children. Hess has shown a similar effect from yeast. The dosage is not yet satisfactorily worked out, and the conditions under which the effect is produced are not yet defined.

(Emmett and McKim[54] from studies on pigeons conclude "that there are apparently two so-called vitamins associated with rice polishings, one of which cures polyneuritis and one of which produces weight, and of these two, the Seidell yeast vitamin preparation (prepared with Lloyd's reagent) contains chiefly the curative fraction, along with a small percentage of the other." Funck found Seidell's vitamin preparation from autolyzed yeast with Lloyd's reagent was greatly deficient in the growth stimulant and had lost some of its antiscorbutic power.)

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[54] Emmet, A. D., and McKim, L. H.: The Value of the Yeast Vitamin Fraction as a Supplement to a Rice Diet. Jour. Biol. Chem., 1917, **32,** 3.

Gerstenberger,[55] in a lengthy article, covers much recent literature on scurvy and offers an hypothesis regarding its pathogenesis. He imagines that all the symptoms of scurvy as we know them today (hemorrhage into the bones and tissues, rarefaction and swelling of the osseous system, exaggerated reflexes, tachycardia and dilatation of the heart, and hyperesthesia) may be explained "on the common basis of a primary or secondary interference with one or more of the normal functions of calcium, alone or in conjunction with its physiologic anion, a condition which he is pleased to call *a partial defunctioning of calcium and its physiologic anion;* that in scurvy as we see it occur in infants this defunctioning is caused by a substance produced through a break in the metabolism of carbohydrates, whatever their original source may be; that the break occurs as the result of the absence or inactivity or relative insufficiency or inadequacy of some physiochemical substance or "vitamin" essential to the establishment and performance of normal carbohydrate metabolism; that the defunctioning substance possibly is oxalic acid or some other agent that has a similarly strong affinity for calcium, and that after combining with calcium is soluble with similarly great difficulty.

Comby[56] calls attention to the injurious effects on infants of a diet that is low in butter fat. This has become an important matter owing to the diminished fat ration of warring peoples. The effect of giving too much fat in the diet of infants is the production of colic, vomiting, and diarrhea, as is well known. A diet that is continuously too low in fat may lead to two forms of disturbance, a general one which is termed by Comby *dystrophie adipogénétique,* and a local one attacking the eye, *xérophthalmie.* The latter is often the local manifestation of a more general condition. C. E. Bloch[57] (Denmark) has recently described 40 cases of xerophthalmia. Dryness and wrinkling of the conjunctivae is the first noted, then the appearance of bluish white spots that give the name xerosis. The affection progresses, the conjunctiva becomes insensible; necrosis sets in. In other cases the activity of the process is shown by the appearance of dacryorrhea and photophobia.

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[55] Gerstenberger: Pathogenesis of Infantile Scurvy: An Hypothesis. Am. Jour. Med. Sc., 1918, **155,** 253.

[56] Comby, J.: La diete maigre chez les nourrissons. Arch. de méd. d. enf., 1918, **21,** 313.

[57] Bloch, C. E.: Cited by Comby, note 56.

The more general affection assumes three forms: (1) a general atrophy, athrepsia; (2) a dystrophic form, and (3), in children of a year or more, a universal dystrophic process in which the volume corresponds to the age and there is no abdominal distention but there is excess pallor and considerable emaciation. The cutaneous surfaces may be white and dry, and exhibit dermatitis.

These conditions have long been known in Japan, where they have been attributed to the use of a dietary that is deficient in fat, and treated by administering cod liver oil. Mori[58] described the condition under the name of *hickan* and has given statistics on many cases (1899-1904).

Reaction of Mouth.—The power of the saliva to maintain a protective function over the teeth against dental caries has been long a subject of investigation but little has been proved. Miller, in 1891, attributed a strong alkaline reaction to the animal saliva and a great content of carbonate of the alkalies that might neutralize acids, thus tending to prevent the appearance of caries. Marshall, in 1915, stated that saliva is amphoteric, and that therefore for it to be a factor in protecting the teeth it must neutralize either acid or alkaline substance as taken into the mouth, and that it is the degree of this power to maintain a neutrality in the mouth which is indicative of susceptibility to caries. Gies and co-workers could not substantiate this.

Howe and Keniston[59] have sought to find out what relation there may be between the salivary factor of Marshall and the incidence of dental caries. The work is from the laboratory of the Forsyth Dental Infirmary for Children, in Boston. They find that the saliva of persons immune to dental caries varies, as does that of persons with carious teeth. Their tables do not show consistently that as the difference between the total neutralizing power of resting and activated saliva diminish, liability to incidence of caries increases. There is doubt as to the importance of the salivary factor.

Rongel[60] has studied the modification of the mouth reaction in infants on different diets.

Air Swallowing.—In a lengthy article Kantor[61] points out that, although the symptoms associated with gas in the digestive tract—

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[58] Mori: Cited by Comby.

[59] Howe, Percy R., and Keniston, Mildred R.: The Salivary Factor in Relation to Dental Caries. Am. Jour. Physiol., 1918, **46,** 28.

[60] Rongel: Arch. de méd. d. enf., 1918, **21,** 27.

[61] Kantor, John L.: A Study of Atmospheric Air in the Upper Digestive Tract. Am. Jour. Med. Sc., 1918, **155,** 829.

belching, tympany, ameteorism, flatulence, etc.—have been the subject of comment from earliest times, it has most commonly been taken for granted that the gases in question have their origin entirely within the body, whether from the decomposition of food, exhalation of vapors, or from the interplay of gas-producing juices. He reviews the general historical background of the subject. The ancients elevated the condition to the dignity of a definite disease entity, *morbus ructuosus*. It was not until after the studies of Van Helmont (1652) and near the end of the eighteenth century that the indefinite notion of morbus was abandoned. Interest then centered on the actual composition and origin of the gases themselves. Magendie (1813) gave the first clear account of air swallowing in his report of the case of a conscript who practiced auto-inflation in order to avoid military service. Chevillot (1833) made careful quantitative studies on the gases of man in health and disease. After 1865, German investigators expanded their studies until the whole subject of gastric fermentation and putrefaction was covered, not only from its chemical aspect, but from the bacteriologic and general clinical point of view as well (Naunyn, Hoppe-Seyler, Boas, and others). The more normal behavior and source of gastric gases was studied by Planer, Yllpö, and others, the general trend of whose work was toward the belief that the basis of gastric gases under normal conditions is constituted by atmospheric air, modified, however, by certain definite processes.

Magendie had pointed out that air swallowing was akin to the "cribbing" of horses, that the condition was by no means a rare one, and that it could be acquired by practice. He taught students to do it and made the first attempt to describe the mechanism of the act.

In spite of this work it was never fully realized that air swallowing is a perfectly normal physiologic process, and one that under pathologic conditions may give rise to disturbances that are generally assumed to be due to gases originating from the body. Quincke (1899) and later Bouveret gave complete expression to this viewpoint, and the latter suggested the term "aerophagia," which has been generally adopted. Much later work has followed. That by Smith and Le Wald[25] covering the condition in infants was reviewed two years ago.

Kantor considers briefly the composition of the gas found in the stomach of the adult, and the entry of air into the stomach. Air enters the stomach in one of two ways: It may either be carried down with fluids or solids in ordinary swallowing, or it may be "gulped" down alone. Both methods are carefully studied with the help of the fluoroscope.

Modern investigation has shown that in the act of swallowing "we are dealing with an orderly progression of pressures and inhibitions which may be presented as far as they are known, schematically, as follows: A. Pressures: (1) initial buccopharyngeal thrust (Meltzer and collaborators); (2) esophageal peristalsis (Magendie, etc.). B. Inhibition: (1) inhibition of esophagus mouth (Killian); (2) relaxation of esophagus (Schreiber); (3) inhibition of cardia (Meltzer); (4) receptive relaxation of stomach (Cannon). This brings into greater prominence the part played by the cardia. The act is divided into three periods, instead of the classic two, and these three periods are the buccopharyngeal, the esophageal, and the cardiogastric.

Kantor describes in detail the act of air swallowing, which he practices himself, and has taught to others. In general it is much easier to swallow air in the recumbent than in the standing position.

The greater part of the air introduced into the stomach escapes through the esophagus by eructation. Closer observation shows that a very large number of people eructate. Kelling has found that in adults belching occurs whenever the intragastric tension reaches 25 cm. of water. Gastric tension is low at the time of swallowing and rises (Dobrovici) as digestion progresses. Individual sensitiveness to the presence of gas in the stomach, posture, gastric acidity, and peripheral reflexes all play a part. Aerophagia may be associated with eructation, and all persistent belchers should be regarded clinically as air-swallowers.

Air remaining in the stomach increases in bulk (as much as 12 per cent. in winter) through expansion due to the greater internal temperature. Its bulk diminishes in the digesting stomach owing to the absorption of oxygen—approximately 12 c.c. per minute (Yllpö). Air swallowed on an empty stomach may pass the pylorus, as shown by the fluoroscope.

De Buys and Henriques[62] report the result of some fluoroscopic examinations of the child's stomach, showing the effect of body posture in its position and emptying time. Active peristalsis in the stomach was noted in their youngest patient, aged 4 months. In one of their cases the adult type of stomach was reached at 3 years. The position of the stomach and especially the position of the solid contents of the stomach was found to be influenced by body posture. Motility of the stomach is most rapid in the right lateral position. The supine position produces a comparatively slow motility.

(To be continued)

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[62] De Buys, L. R., and Henriques, A.: Effect of Body Posture on Position and Emptying Time of Stomach. Am. Jour. Dis. Child., 1918, **15,** 190.

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STANDARDS FOR GROWTH AND NUTRITION *

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The widespread interest lately aroused in the prevalence and degree of malnutrition among school children makes it desirable to examine anew the facts of normal growth in this class of our population. The existence of undernourishment or malnutrition presupposes a normal standard which must be reached if a child is to be considered in perfect health.

The standards by which nutrition has been chiefly measured in the past have been the body-weight and the rate of increase in weight as compared with normal averages. Height and rate of growth in height have also been given a certain amount of value. Most observations have considered both height and weight in relation to the age of the child. The purpose of this paper is to show that the weight-to-age and height-to-age relationships are of comparatively little value in estimating the nutrition of the body. The relation of weight to height is the only one which is reliable.

The standards of nutrition which are susceptible of application to large groups of children are three:

1. The weight-to-height relationship.
2. The annual rate of increase in weight and growth in height.
3. The general appearance of the child.

In the first two of these it is easy to determine the *average;* not so easy to decide what is *normal.* Considerable variations from the average may coexist with normal nutrition. It is important to understand and appreciate how wide the individual variations may be among healthy children of the same race and living in the same environment. What deviation from the average is to be regarded as abnormal, is a question about which differences of opinion may readily exist. Any

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standard fixed must be an arbitrary one. To consider as undernourished any child who falls 10 per cent. or more below the normal average is a workable standard and may be adopted in practice until further experience throws more light on the subject.

Since the pioneer work of Quetelet many observations have been made both in this country and abroad on the weight, height and growth of children of the different ages of different races and environment. A special interest attaches to this subject at present, since it is the prevailing opinion that the nutrition of children in all the belligerent countries has greatly suffered because of war conditions and the rise in the cost of food.

In this article will be considered only children of the usual school ages, 5 to 16, inclusive, not because these are more important, but because more data are available than for children of the pre-school age. In the charts given we have, for similar reasons, included only those relating to boys.

During the first year of life we have been accustomed to regard the weight as the chief or sole measure of the progress in nutrition. A regular gain in weight is universally considered as the best evidence of proper growth (an exception of course being made in the case of infants fed on certain proprietary foods and others on mixtures abnormally high in carbohydrates). The growth of the infant in length has been regarded of interest chiefly for the recognition of such conditions as affect the growth of the long bones—rickets, cretinism, chondrodystrophy, etc. After the first year growth of the body in length becomes of more and more interest and of increasing importance in relation to normal nutrition and growth, but it has not received the attention which it should.

Weight and Age Variations.—By far the largest number of observations on weight published have been of weight in relation to age, and the opinion has gained currency that a child of a certain age should have a certain weight to be normal, a moderate latitude for individual variations being allowed. Since most observers give only the *average* weight of children of the different years, it is somewhat difficult from their figures to estimate for the individual variations.

In Chart 1 are given the actual net weights of boys in the Browning School[1] in New York City. It represents 1,774 observations on about 350 different boys whose weights were taken semi-annually, without clothes, over a period of years, the average number of observations on each boy being five. This group of American boys, with but few

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[1] I wish to express my thanks to Mr. John S. Browning, headmaster of the school, for the use of these data, and also to Dr. C. M. Williams, physical director, by whom most of the weights and measurements were taken.

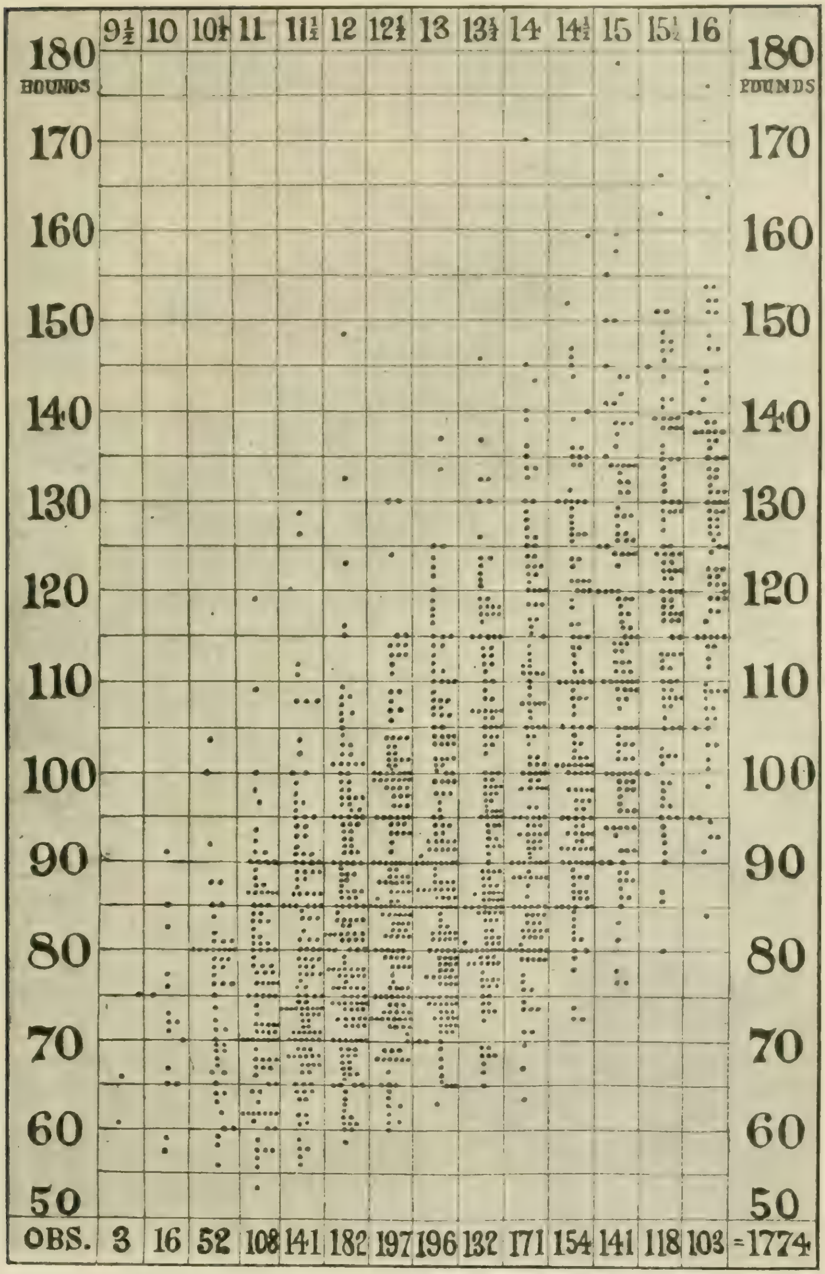

Chart 1.—Age and weight. Boys from the Browning School; 1,774 observations on 350 boys.

exceptions, came from wealthy families and had had the advantage of good care and proper food all their lives. How wide the variations are for the different ages is seen from a glance at the chart. Omitting the few very high and the few extremely low weights, we note that the individual variations for the different years are approximately as shown in Table 1.

TABLE 1.—Weight-Age Individual Variations (Browning Boys)

At Age	Range, Pounds	Variation, Pounds	Years' Growth, Approximately
11	60- 90	30	5
12	65-105	40	5
13	70-115	45	5
14	78-125	47	4
15	90-140	50	3½

These extreme variations in healthy boys of the same social class show how hard it is to fix on a standard weight for any age. In this series slightly more than one-fourth the boys were more than 10 per cent. below the average weight of the group for the age.

It is interesting to compare these figures with those of Bowditch[2] for Boston public school boys of corresponding ages. Omitting here also the few extremely high and extremely low weights we have the results set forth in Table 2.

TABLE 2.—Weight-Age Individual Variations (Bowditch Boys)

At Age	Range, Pounds	Variation, Pounds	Years' Growth, Approximately
5	32- 52	20	5
6	36- 56	20	4
7	40- 60	20	4
8	44- 64	20	4
9	48- 72	24	4
10	52- 76	24	4
11	56- 84	28	5
12	60- 96	36	4½
13	64-108	44	5
14	68-116	48	4
15	84-128	44	3½
16	96-142	46	3

His observations average about 350 for each year of age. Nearly one-fourth of these boys (23.2 per cent.) were 9.3 per cent. below the average weight for the age, while one-tenth of his boys were 17.2 per cent. below the average weight of the group for the age.

When we come to compare the observations[3] upon weight and age

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[2] Bowditch: Growth of Children, Public Document, Massachusetts State Board of Health, 1877.

[3] The data from which the curves in this paper have been constructed are taken from U. S. Bureau of Education, Bulletin 10, 1914, by Bird T. Baldwin. In this will be found a very extensive bibliography on the growth of school-children.

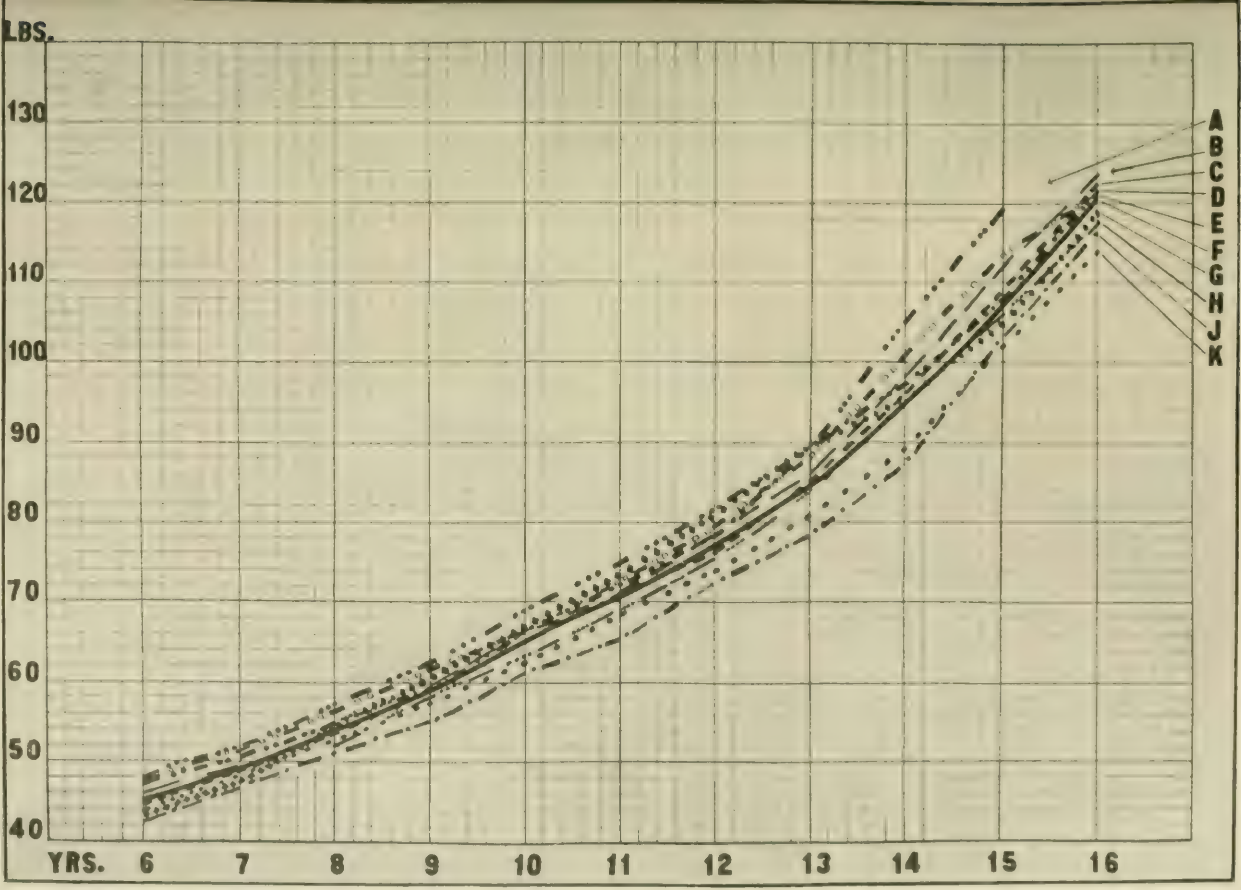

Chart 2.—Weight and age. American boys.

	Approx. No. Observations
A. Boas, California	1,900
B. West, Worcester, Mass.	1,500
C. Peckham, Milwaukee	4,000
D. Barnes, Oakland, Calif.	2,500
E. McDonald, Washington, D. C.	7,000

	Approx. No. Observations
F. Bowditch, Boston, Mass.	13,000
G. Baldwin, Chicago and New York	100
H. Smedley, Chicago	2,500
J. Hastings, Nebraska	7,000
K. Porter, St. Louis	16,000

made in different parts of the United States and those made in foreign countries with the foregoing we see how wide the average weight-age variations are.

In Chart 2 are given the average weight curves of ten different series of observations on American schoolboys made in widely scattered parts of the country. These represent in all nearly 50,000 observations. The lowest average curves are "J," that of Hastings, and "K," of Porter; the highest average is "A," that of Boas. The solid black line, "F," of Bowditch, is very nearly the mean of the entire group, and may therefore perhaps be taken, as well as any single curve can, as the average curve of the country as a whole.

It will be noted that the variation in these curves, which represent averages, at 6, 7 and 8 years is only about 5 pounds; also that this variation steadily increases with the age, so that at 14 and 15 years it is about 15 pounds. There is, however, a general parallelism to the curves, indicating that the rate of gain is nearly the same in the different groups.

When Chart 2 is compared with Chart 3 it is evident what a large part nationality plays in modifying a weight-age curve. The observations in Chart 3, like the others, were made on boys in public schools. The heaviest boys for their ages are Russians and Polish (A and B). The lightest are Japanese (H); then in order come the Italian in Italy (G); Italian in the United States (K), and the German (J). Even omitting the Japanese, we see how wide is the variation in the weight-age curve among the European nations, all of which are represented in our present American population. With such wide variations as those noted both in foreign and in American boys it is evident that weight for age is not of great importance in determining the nutrition of a child.

Height and Age Variations.—The curves for height and age in a general way correspond to those of weight and age among the different groups in the United States and also among the foreign boys in their relation to each other, but the variations in the height-age curves are considerably narrower.

Chart 4 shows the variations in a group of boys of the same nationality and the same social environment — the boys of the Browning School. Omitting the few extremely high and extremely low measurements we note in Tables 3 and 4 the range and variation in height.

Both these groups show how wide are the individual variations met with in boys of the same general class. By comparing these tables with the weight-age Tables 1 and 2, it will be seen that, estimating in years' growth, the differences in weight among individuals are less

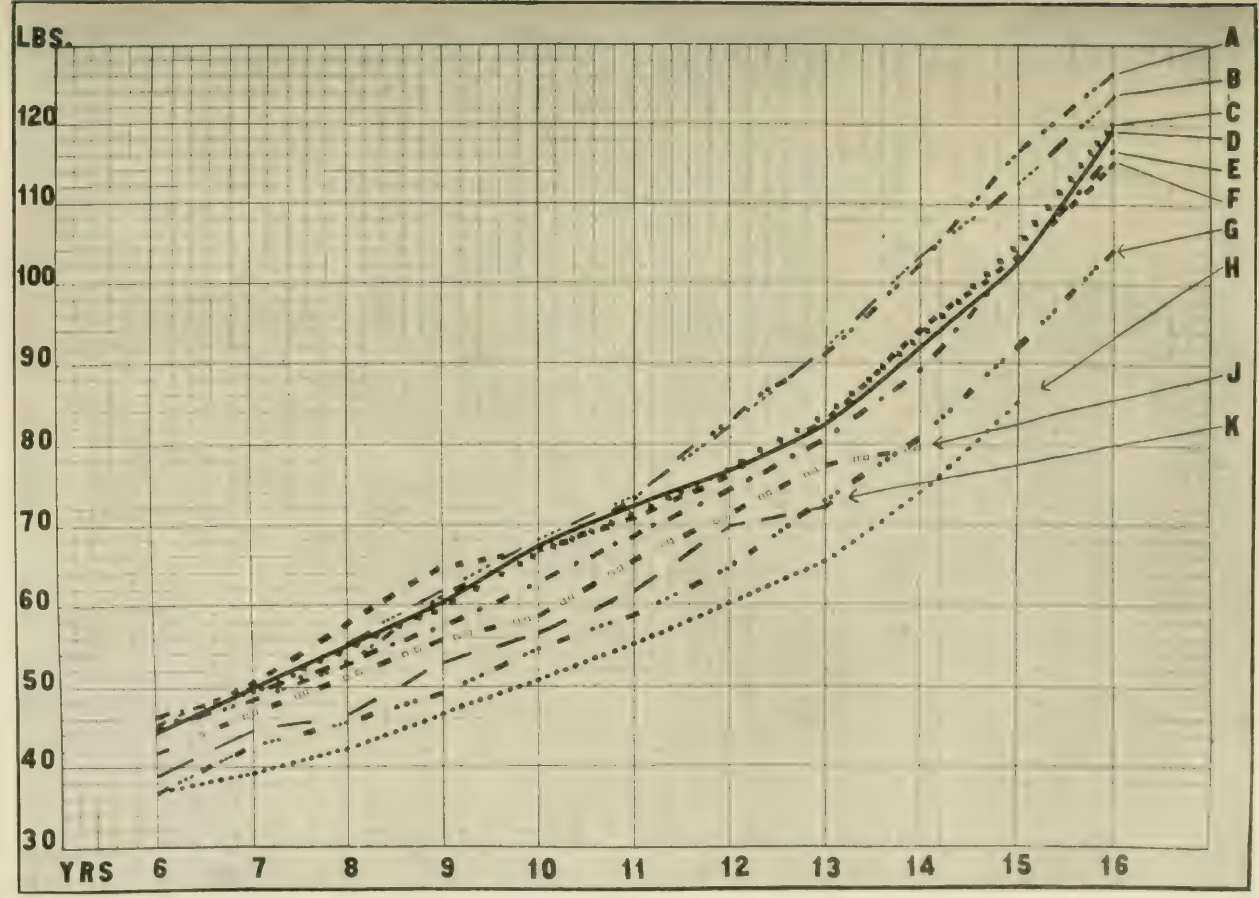

Chart 3.—Weight and age. Foreign boys.

	Approx. No. Observations
A. Erismann, Russian	2,450
B. Suligowski, Polish	1,250
C. Stevenson, British	.....
D. Roberts, British	25,000
E. Hertel, Danish	17,000
F. Key, Swedish	14,000
G. Pagliani, Italian in Italy	900
H. Misawa, Japanese	9,000
J. Schmidt, German	4,700
K. Hrdlicka, Italian in U. S.	.....

than the differences in height, and that in both weight and height as boys approach maturity these differences tend to become less.

In Chart 5 are given the height-age curves of the American boys whose weights are given in Chart 2. It will be seen how closely these curves of average height of different groups correspond.

Only one, "A," Baldwin's, differs in any important degree from the average; "K," Porter's curve, is a little lower than the others; and "B," West's curve, a little above. The curves of the other seven observers are almost identical. The solid black line, "D," is the curve of Bowditch. This line may therefore be taken as a fair average of school boys of the United States.

TABLE 3.—Height-Age Individual Variations (Browning Boys)

At Age	Range, Inches	Variation, Inches	Years' Growth, Approximately
11	53-60	7	3
12	55-62	7	3
13	58-64	8	2½
14	59-67	9	2½
15	61-70	9	2
16	62-72	8	2

TABLE 4.—Height-Age Individual Variations (Bowditch Boys)

At Age	Range, Inches	Variation, Inches	Years' Growth, Approximately
5	38-44	6	3
6	40-46	6	3
7	42-49	7	2½
8	44-51	7	2½
9	46-53	7	2½
10	48-55	7	2½
11	49-57	8	2½
12	50-60	10	3
13	52-62	10	3
14	54-65	11	3
15	57-67	10	2½
16	60-70	10	2½

In Chart 6 are given the curves showing average heights at the different ages of various foreign groups of boys. The variations are almost as great as are seen in the average weights of these boys, and in a general way the curves of weight and height correspond. It is clear, then, that in height as well as in weight, race must be taken into account in determining the normal average.

When very large groups are considered, the increase in height and in weight goes on together proportionately in children who are perfectly healthy. When smaller groups or individuals are closely observed it is seen that growth in height is, with the majority, more irregular than the increase in weight and is influenced by many conditions about which as yet we know very little. In private practice

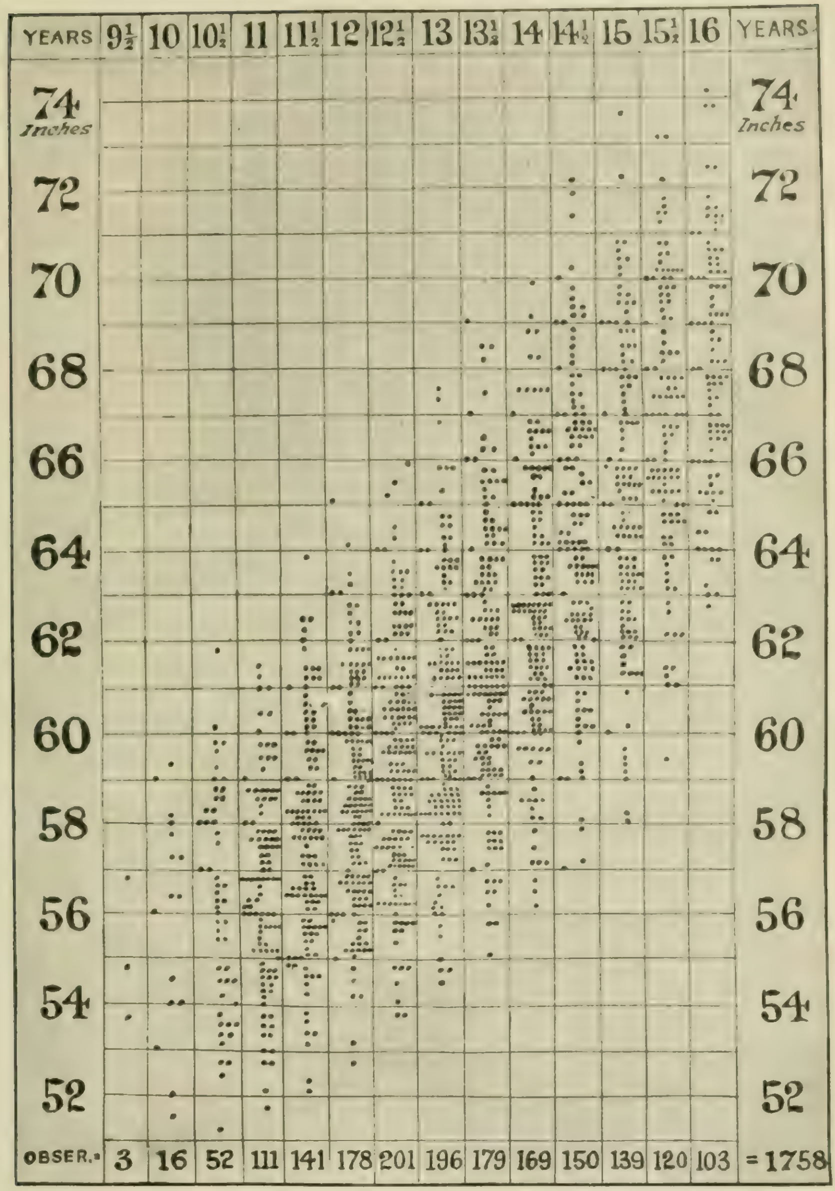

Chart 4.—Age and height. Boys from the Browning School; 1,758 observations on 350 boys.

one is constantly impressed with the great influence of heredity as affecting growth in height. This is a factor the importance of which it is difficult to estimate when large numbers of school children are measured. The variations in height are so great that it is difficult to say how wide a deviation from the average may be considered abnormal even in the same race and social status. In the young the impulse to grow is so strong that even when food is insufficient it may continue, the increase in height taking place at the expense of the stored-up materials in the body. It may be coincident with no increase in weight or even at times with actual loss in weight. As a guide to a child's nutrition, height-age curves are therefore quite unreliable.

Weight-to-Height Variations.—A much more important relationship than weight-to-age or height-to-age as an indication of the state of the child's nutrition is that of the weight-to-height. The value of this is recognized by all the insurance companies. What an adult man or woman should weigh for his or her height is brought to our notice constantly by the figures given on the penny-in-the slot scales. In childhood less attention has been paid to this relationship than its importance deserves, and even though here there are no absolute figures of weight-to-height which can be regarded as normal, and there are considerable individual variations seen in healthy subjects, yet these variations from the average are not so great but that they furnish important information regarding the nutrition of the child.

Considering how wide is the variation seen in different races in the height and weight of boys of the same age, it is rather surprising to see how nearly alike are the curves of weight-to-height. This is shown in Chart 7, which gives the weight-to-height curves for boys from five different nationalities; the two tall and heaviest (Russian and Polish), the two small and lightest (Italian and Japanese) and the American, using Bowditch's figures for Boston school boys of American parentage.

That these curves are so nearly alike indicates how independent of nationality is this index of nutrition. Thus, the average Japanese boy of 50, 60 and 80 pounds is only one inch shorter than the average American boy of the same weight; while those of 70 pounds weight appear exactly the same height. So, also, the Italian boy, who, though much shorter than the American for his age (Chart 5), is for his weight only from half an inch to an inch shorter than the American up to a weight of 105 pounds and a height of 62 inches; the only exception to this being the short period when the weight is in the neighborhood of 50 pounds and the height near 50 inches. The chief difference between the tall and short races is that in the latter growth is slower and ceases at an earlier period.

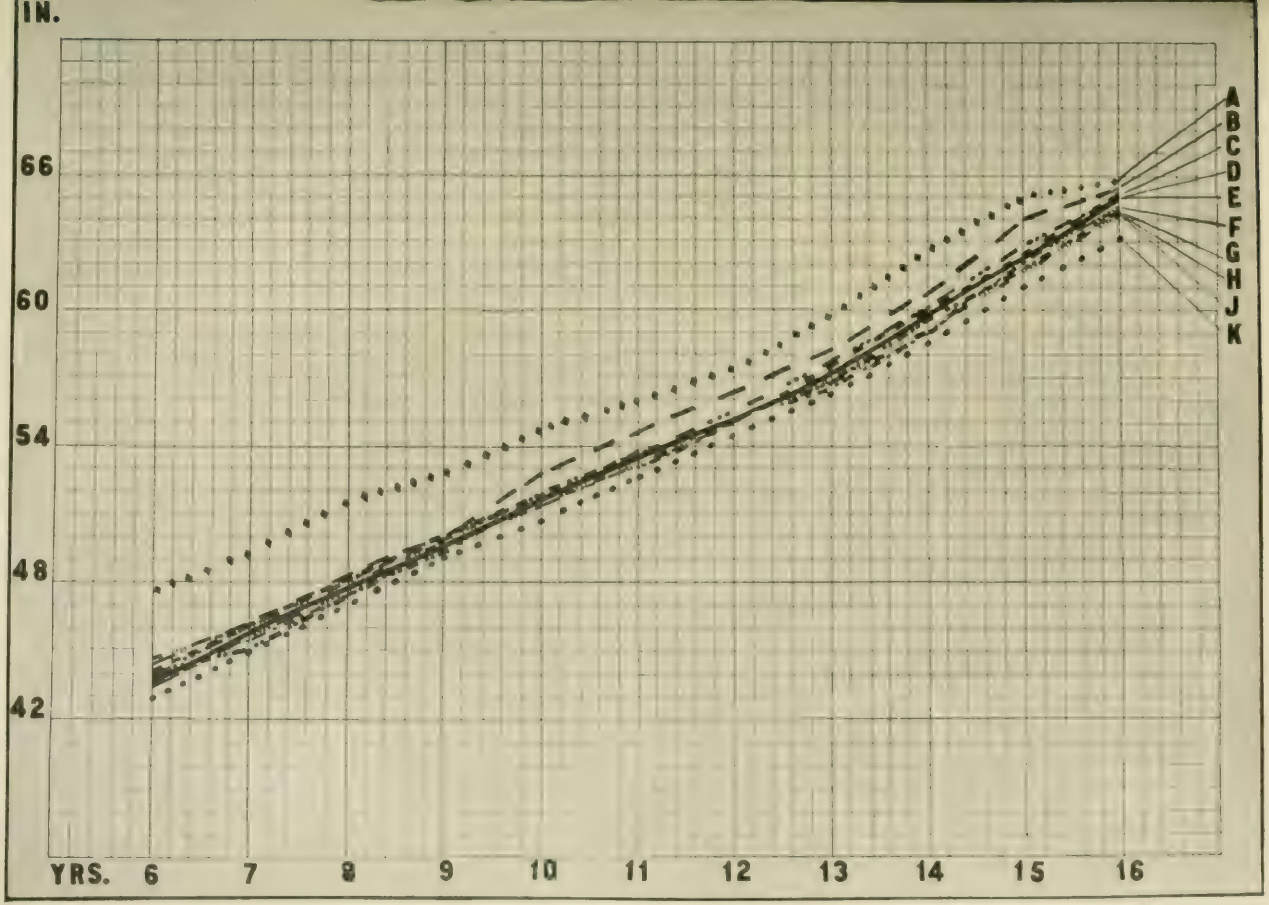

Chart 5.—Height and age. American boys.

	Approx. No. Observations
A. Baldwin, Chicago	300
B. West, Worcester, Mass.	1,500
C. Peckham, Milwaukee	4,000
D. Bowditch, Boston	13,000
E. Boas, California	44,000
F. Smedley, Chicago	2,500
G. Barnes, Oakland, Calif.	2,500
H. Hastings, Nebraska	7,000
J. McDonald, Washington, D. C.	7,000
K. Porter, St. Louis	15,000

Weight-Height Index.—The determination of where a child stands in the relation of his height to his weight is undoubtedly the best simple guide in fixing his status as to his nutrition. This ratio expresses the general solidity or robustness of the body and is therefore significant. The weight in kilos divided by the height in centimeters, or weight in pounds divided by height in inches gives what is sometimes called the *weight-height coefficient* or *weight-height index* of the individual. This weight-height index increases steadily and quite uniformly from 5½ up to 18 years. According to the observations of Baldwin, the lowest weight-height index in boys is at 6 years, when it is 0.15; the highest is at 17½, when it is 0.40.

The same thing is shown in another way in Table 5, the data for which are taken from Bowditch. Here is given the increase in weight which corresponds to each inch increase in height.

TABLE 5.—Weight-to-Height Increase

	Boys			Girls		
Height, Inches	Weight, Pounds	Increase Per Inch, Pounds	Approx. Age, Years	Weight, Pounds	Increase Per Inch, Pounds	Approx. Age, Years
42	41.8	...	5	40.9	...	5
43	43.6	1.8	..	42.6	1.7	..
44	45.6	2.0	..	44.5	1.9	..
45	47.6	2.0	6	46.5	2.0	6
46	49.6	2.0	..	48.5	2.0	..
47	52.1	2.5	7	50.7	2.2	7
48	54.6	2.5	..	53.2	2.5	..
49	57.3	2.7	9	56.1	2.9	9
50	60.2	2.9	..	58.8	2.7	..
51	63.2	3.0	10	61.4	2.6	10
52	66.3	3.1	..	64.4	3.0	..
53	69.2	2.9	11	67.5	3.1	11
54	72.7	3.5	..	71.0	3.5	..
55	76.4	3.7	..	74.9	3.9	..
56	80.2	3.8	12	78.8	3.9	12
57	84.0	3.8	..	83.4	4.6	..
58	87.9	3.9	13	87.9	4.5	..
59	91.6	3.7	..	93.3	5.4	13
60	95.5	3.9	..	98.8	5.5	..
61	100.5	5.0	14	105.4	6.6	..
62	105.6	5.1	..	115.7	10.3	14
63	110.7	5.1	15	.....	....	..
64	115.9	5.2	..	....	....	..
65	121.0	5.1	16	....	....	..
66	126.6	5.6	..	.....	....	..
67	136.1	9.5	..	...	....	..

In all observations on weight and height of children the *average* is not to be confused with or regarded as the *normal*. There are considerable variations on either side of the average which should be regarded as within the range of the normal. The normal is a zone, not a line. How far below the average weight for his height a child should be for his nutrition to be considered below the normal, one cannot say

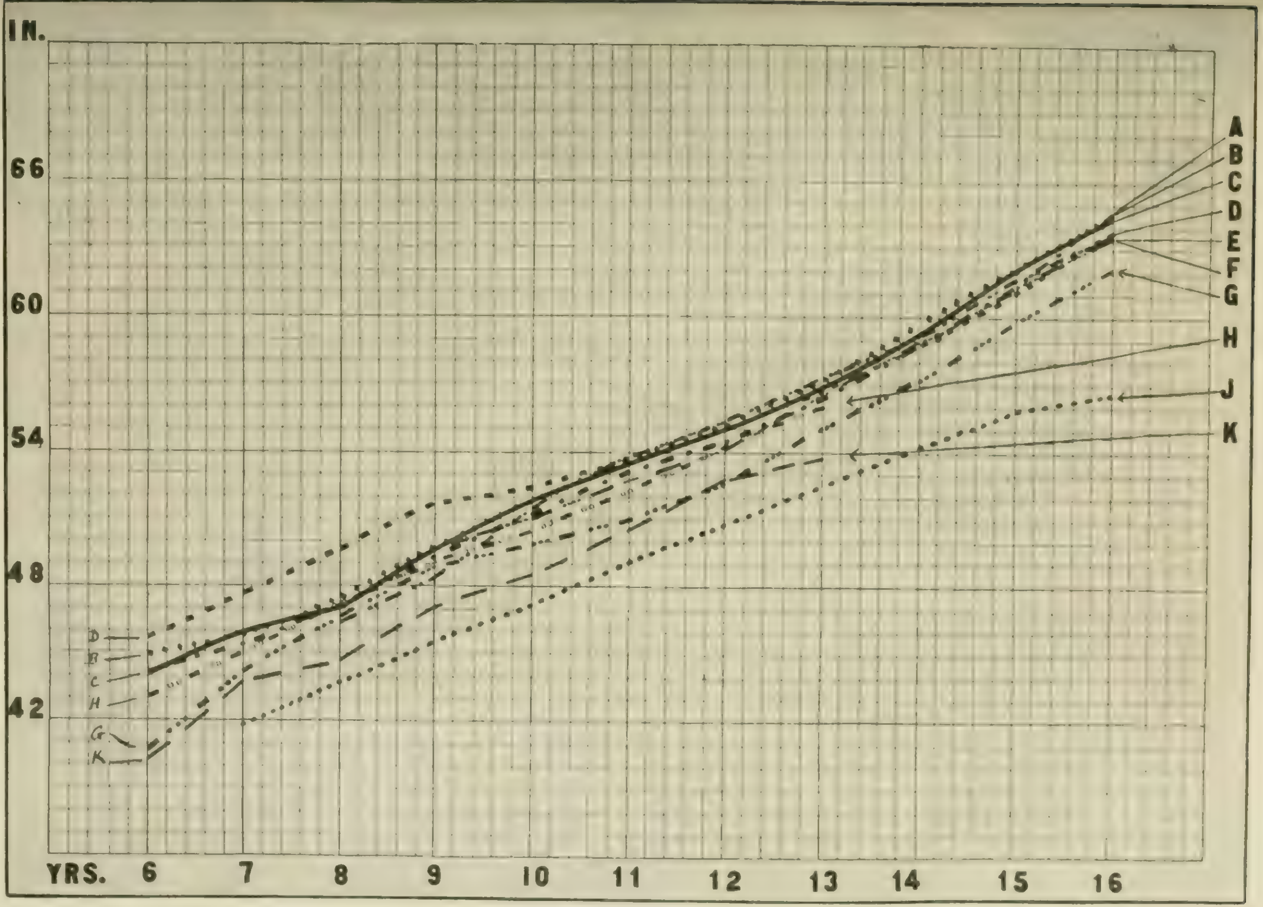

Chart 6.—Height and age. Foreign boys.

	Approx. No. Observations		Approx. No. Observations
A. Hertel, Danish	17,000	F. Suligowski, Polish	1,000
B. Stevenson, British	.....	G. Paghani, Italian in Italy	900
C. Roberts, British	25,000	H. Schmidt, German	4,700
D. Key, Swedish	14,000	J. Misawa, Japanese	9,000
E. Erismann, Russian	3,000	K. Hrdlicka, Italian in U. S.	.....

absolutely. If we regard all those who are 10 per cent. or more below the average line as undernourished or as examples of malnutrition, we shall not go far wrong. For practical purposes we may assume this to be correct.

Annual Rate of Increase in Weight and Height.—The weight to height relation we have concluded to be the best general starting point or base line for observations on the nutrition of children;[4] but nothing indicates their progress so well as the annual increase in height and weight. Like an infant, a boy or girl to be healthy must grow; and a record of such growth of any child extending over a period of years will be found to be an accurate and trustworthy record of his general health during that period.

The annual rate of gain of healthy school boys of corresponding ages is nearly the same in different parts of the United States and in foreign countries. In the accompanying table (6) is given the average annual gain in weight and height of American boys and girls, calculated from the data represented in the curves previously given. It will be noted that in the boys the gain in weight increases with each year of age after 7 years, except between 10 and 11, when it is less than for the preceding period. This slowing up in growth before the marked increase of approaching puberty is noted in nearly all the different groups of boys observed.

The yearly increment in height is less between the tenth and twelfth years than before or after this period. Like the increase in weight, it is least between 10 and 11 years. It does not show a marked increase until after 12, when the rapid growth of puberty begins. This is about a year later than the more rapid increase in weight.

As children grow older the increase in height and weight is less uniform and regular. There are seen with nearly all healthy children periods, often of several months' duration, in which growth and gain in weight are rapid, followed by periods in which both are much slower. This may occur where no special cause can be discovered. It is often seen as puberty approaches.

Children who are much below normal weight usually gain rapidly when the cause for the low weight can be discovered and removed.

Seasonal Growth.—The question is often discussed during what season of the year the most rapid growth in height and increase in weight occur. The observations made on the Browning boys are of interest as throwing some light on this point. Of 703 observations

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[4] There are some exceptions to this rule. Certain children, not a large group, may be stunted in growth by conditions which also affect weight, so that the relation of weight to height is average, though the child is much below the normal in both.

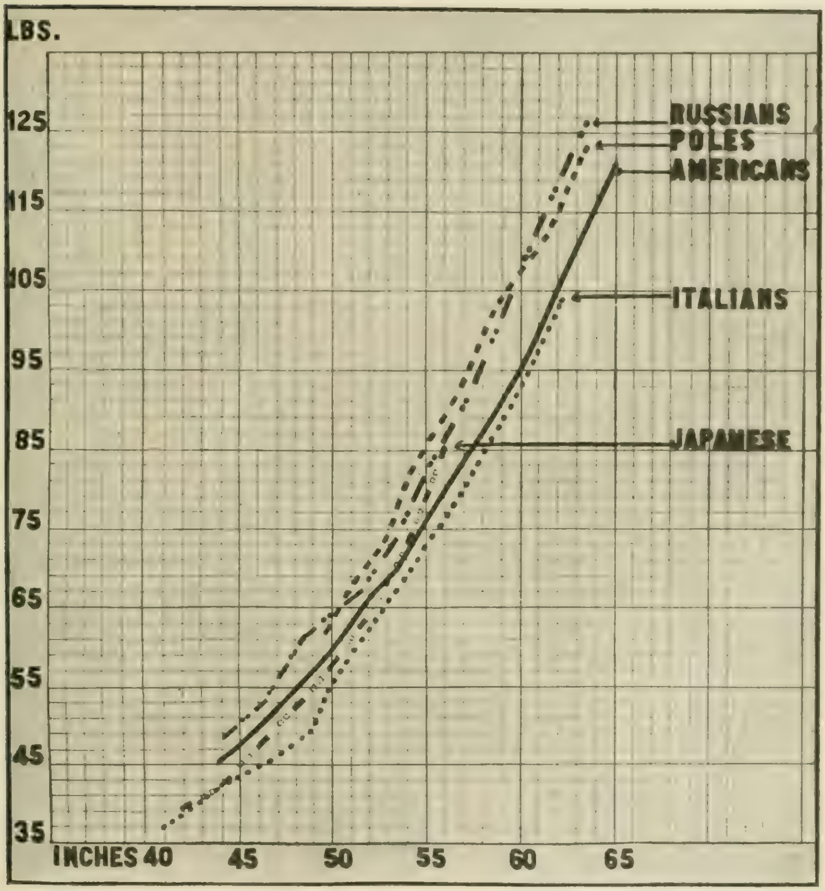

Chart 7.—Weight and height.

made on weight for the six months from November to May and from May to November, the average gain for the summer six months was 1¼ pounds greater than for the same boys during the winter six months. The same thing was seen in growth in height. Of 544 observations made on height, the average increase was 0.36 inch greater for the summer six months than for the same boys during the winter six months. These facts confirm the general law that in healthy indivividuals increase in weight and growth in height go on together and approximately at the same rate.

TABLE 6.—Average Annual Increase in Weight and Height at the Different Ages

BOYS

	Weight		Height	
Age, Years	Range, Pounds	Average, Pounds	Range, Inches	Average, Inches
6- 7	3 - 5	4	1.5-2.5	2
7- 8	3.5- 5	4.75	1.5-2.5	2
8- 9	4 - 6	5.25	1.5-2.5	2
9-10	4 - 7	6	1.5-2.5	2
10-11	4 - 6.5	5	1.4-2.0	1.7
11-12	4.5- 7.5	6.5	1.3-2.0	1.8
12-13	6 - 9	8	1.5-2.5	2
13-14	8 -12	10	2 -3	2.5
14-15	10 -15	12.5	2 -3.5	2.7
15-16	9 -15	13.75	2 -3.5	2.7
16-17	4 -12	6.5	0.5-2	1.2
17-18	4 - 8	5	0 -1	0.5

GIRLS

	Weight		Height	
Age, Years	Range, Pounds	Average, Pounds	Range, Inches	Average, Inches
6- 7	3 - 5	4	1.5-2.5	2
7- 8	2 - 5	4.5	1.5-2.5	2
8- 9	3.5- 6	5	1.3-2.4	1.75
9-10	4 - 6	5.25	1.5-2.5	2.25
10-11	4.5- 7	6.5	1.5-2.5	2
11-12	7 -11	9.5	2 -3	2.5
12-13	8 -12	10.5	2 -3	2
13-14	7 -11	9.5	1.3-2.4	2
14-15	5 -10	7.5	1 -2	1.25
15-16	3 - 8	6	0 -1	0.75
16-17	2 - 6	3.5	0 -0.5	0.50
17-18	0 - 2	0.5	0 -0.2	0.2

The explanation for more rapid growth during the summer season would seem to be that this period includes the school boy's vacation time, during which he leads a more free and more outdoor life; while the winter period includes most of the colds and other respiratory diseases and a large part of the contagious diseases from which those of these ages are likely to suffer, all of which arrest growth and gain in weight.

General Appearance.—In estimating a child's condition as to his nutrition, careful inspection may tell a good deal, particularly to an experienced observer. The color of lips and cheeks and the facial expression are significant of anemia, fatigue or even exhaustion. If the clothing is removed to the waist, the muscular development and the amount of subcutaneous fat can be determined as well as a narrow chest and round shoulders recognized. Such an inspection taken in connection with height and weight enables the examiner to form a pretty accurate estimate of the child's nutrition.

The so-called Dunfermline scale in which children are graded in their nutrition by their appearance as I, good; II, fair; III, below average; IV, very bad, is not a very trustworthy way of estimating the nutrition if such inspection is made without undressing the child at all and without taking account of height and weight. But taken in conjunction with height and weight and when made by a person of experience, the general appearance is of great assistance in grading the child, and the grouping in the above scale is very convenient for practical purposes.

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EXPERIMENTAL RESEARCH ON THE EFFECT ON THE GASTRO-INTESTINAL TRACT OF THE EXCRETION OF POISONS, CONSIDERING THE AGE OF THE ANIMALS *

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It is well recognized that a part of the poisons absorbed by the blood is excreted in the gastro-intestinal tract and produces a certain effect on its mucous membrane. However, systematic histologic experiments concerning these effects are lacking, and especially as regards the differences of effect between grown and very young animals.

From my experiments I expected: (1) that the various kinds of poisons offered would produce different effects on the different regions of the intestinal tract; (2) that the pathologic-anatomic and pathologic-histologic study of these effects would show various results, depending on the kind of poison used; (3) that in such experiments the results obtained would differ to a certain degree in very young animals from those in grown animals.

It is certain that in diseases of the intestinal tract of infants the clinical signs and the pathologic-anatomic findings usually differ from those of the adult. For instance, we know that nutritional disturbances or the enterides of infancy are not localized in the intestine, as is the case with adults, but are accompanied by a general affection, causing severe disturbances in the general metabolism; however, contrary to expectation, the postmortem examination shows no such violent changes in the intestinal mucosa. Again, we know that dysentery, an infectious disease of the intestinal tract, often runs in infancy an atypical course, and pathologic-anatomic changes are not distinctly localized in the large intestine, as is usually the case in the adult, but often extend to the small intestine.

Experimental pathologic research concerning the above points seems to be lacking. In my experiment it was purposed to compare the function of the gastro-intestinal mucosa, in regard to the excretion of poisons, and the change produced thereby, in the intestinal mucosa of very young animals with that found in grown animals.

METHOD

The poisons used were, 1 per cent. colloidal bismuth in watery solution; mercury (chiefly from 0.5 to 1 per cent. sublimate sodium chlorid solution); 1 per cent. colloidal silver solution; from 0.1 to 1 per cent. arsenous acid solu-

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* From the Department of Pediatrics, Red Cross Society Hospital.

tion; from 0.3 to 5 per cent. potassium bichromate solution; ricin in physiologic salt solution (0.5 mg.: 10); from 0.2 to 0.5 per cent. cantharidin in olive oil; from 0.5 to 1 per cent. snake poison in glycerin-water solution; sterile emulsion of dysentery (Shiga) bacilli; paratyphoid B; typhoid, and cholera bacilli. These bacilli were cultured in agar mediums for twenty-four hours, and were emulsified in a physiologic salt solution in the proportion of 5 c.c. to one agar tube, and were sterilized for one hour at 60 C.

These poisonous solutions were injected intravenously or subcutaneously into rabbits (grown and very young), white rats (grown), dogs (grown, and very young), chickens (grown, and very young), and pigeons (grown).

The feeding of the animals was arranged according to their physiologic habits. The very young rabbits were nursed twice a day by the mother animals. The very young dogs were fed with cow's milk.

As regards the doses of poisons used, the animals were usually poisoned with a dose in proportion to their weight; however, because the disposition of each animal varied according to kind and age, a dose was often given from which the animal became distinctly prostrated, within a certain number of hours or days.

Method of Examination.—The animals were usually killed and dissected at various stages, such as in the acute stage of poisoning (from a few hours to a few days), or in the subacute or chronic stage (from a few days to usually one or two weeks).

Microscopic sections were made from several parts of the stomach, small intestine, cecum and large intestine, and were generally stained with hematoxylin and eosin. Sometimes a frozen section was examined by itself, or stained for fat by sudan III and sometimes by iron reaction. Moreover, I contrasted the intestinal tracts of normal animals of various ages.

EXPERIMENTS

1. *Bismuth Experiment.*—Findings in *grown animals* (6 rabbits, 4 white rats, 3 dogs, 5 chickens, and 3 pigeons): The important change in the intestinal tract was a brownish-black pigmentation in the mucous membrane of the cecum and large intestine, especially intense in the cecum of the rabbit, rat, and chicken, and in the large intestine and cecum of the dog. Moreover, in the cecum of the rat and in the large intestine and cecum of the dog, a necrotic inflammation was produced in part of the mucosa.

Microscopic examination of frozen sections of these pigmented areas showed a pigmentation in the tissue of the mucosa. The epithelial cells on the ends of the villi contained fine, more or less irregular, brownish-black granules in the protoplasm on the superficial side of the nucleus. The capillary walls near the apex of the villus were brownish-black in color; large migratory cells filled with coarse brownish-black pigments were found here and there in the membrana propria and between the epithelial cells. In some cases, in which the animals were poisoned by large doses, similar pigmentation, but very slight, was also seen in the mucosa of the stomach, especially in the fundus, and just a trace was, rarely, found in the small intestine.

Sawai[1] has proved chemically that this pigment is a sulphur compound of bismuth, and he has shown experimentally that it is the result of excretion, not of resorption.

From the sections stained with hematoxylin-eosin a degeneration and necrosis of the epithelial cells occurred showing granulated or vacuolated protoplasm and figures of karyorrhexis or karyolysis, together with a slight infiltration of round cells in the distinctly pigmented regions. In cases of dogs and rats, a necrosis of the tissue of the mucosa was seen, with some hemorrhage and moderately intensive infiltration in the submucosa, in the lower portions of the intestinal tract. Some catarrhal changes were occasionally found in the mucosa of the stomach and small intestine.

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[1] Sawai: Kyoto Igakuzassi (Japanese), 1916, No. 5.

Findings in *very young animals* (18 rabbits ranging from 3 to 18 days of age, a dog 3 days old, 7 chickens ranging from 3 to 10 days old): In most cases a slight brownish-black coloring was produced in the mucous membrane of the stomach and small intestine, especially distinct in the fundus and jejunum, sometimes extending as far as the large intestine, but here much slighter.

Microscopic examination showed that the pigmentation of the mucosa was more intensive in the stomach and small intestine than in the lower portions.

The mode of excretion of the bismuth was so characteristic that the excreting granules were found moderately diffuse, not only in the surface epithelium, but often in the glandular epithelium of the mucosa; while in cases of grown animals the metal was excreted principally and in more concentrated form by the epithelium on the ends of the villi in the lower portions of the intestine. The pigmentation of the mucous membrane in the cecum and large intestine of very young animals, however, was more intensive in comparison with the findings in the stomach and small intestine of grown animals.

The capillary walls were colored, the pigmentation of the migratory cells was rarer and slighter than in grown animals.

In animals about 3 weeks of age the pigmentation in the lower portions appeared more intensive and was slighter in the stomach and small intestine. In animals 2 months old the findings were similar to those of grown animals.

These different findings, comparing very young animals with grown animals, may be due to the scarcity of sulphur in the intestinal contents of the former. To prove this the following experiment was performed:

An ammonium sulphid solution, or flowers of sulphur, was given to several groups of very young and grown rabbits by esophageal catheter twice a day, and in some cases, also, at the same time *per ani,* soon after the injection of bismuth. On the third or fourth day after this treatment the animals were killed and examined. The pigmentation of the mucosa was found in the very young animals to be most intensive in the stomach and small intestine; while in grown animals the lower region was more distinctly pigmented.

Hence, these differences must have been chiefly due to the different modes of intestinal excretion, according to the age of the animals.

2. *Mercury Experiment.*—Findings in *grown animals* (9 rabbits, 3 white rats, 3 dogs, 6 chickens, and 3 pigeons): The important changes were catarrhal inflammation in the first stage, hemorrhagic inflammation in the second stage, and necrotic inflammation in the third stage, produced in the lower portions of the intestine. All of these changes were especially distinct in the cecum of rabbits, rats and chickens, and in the large intestine of dogs. From histologic examination of the first stage, a degeneration and necrosis of the epithelial cells were revealed, containing very scanty and irregular black pigment (iron reaction negative), especially in the ends of the villi. In later stages a moderate hemorrhage was found, with necrosis of the mucous membrane and with intensive infiltration of round cells in the submucosa or in the muscle strata.

Findings in *very young animals* (13 rabbits ranging from 3 to 20 days old, 2 dogs a few days old, 10 chickens ranging from 3 to 11 days old): A diffuse catarrh in all regions, especially distinct in the stomach and small intestine; sometimes erosions here and there; necrotic inflammation was found nowhere. Histologic examination showed a moderately diffuse degeneration of the epithelial cells; here and there necrosis of the epithelium on the ends of the villi, with more or less hemorrhage and a very slight infiltration of round cells.

In the case of rabbits 3 weeks of age there was a moderate hemorrhagic inflammation in the cecum. The findings in animals 2 or 3 months old were similar to those in grown animals.

Experimenting with *artificial sulphuration,* as with the bismuth cases, a necrotic inflammation in a part of the fundus ventriculi and in the cecum of grown rabbits was found, while a catarrh and erosion in all regions of the intestine were observed in very young rabbits.

It is well recognized that intoxication by mercury produces a diphtheritic inflammation in the lower regions of the intestinal tract. The production of this inflammation, however, is variously explained; for instance, it was thought to be produced by the excretion of the metal (Heilborn[2]); or it might be produced secondarily to a disturbed circulation (Kaufmann[3]); or possibly it was caused by secondary bacterial infection (Virchow[4]). Sawai[1] first proved this inflammation to be caused by the sulphuration of the excreting metals. From my findings, let me say, the excretion of mercury in the intestinal tract of grown animals is most distinct in the lower portions, while in very young animals it is moderately diffuse.

3. *Silver Experiment.*—In *grown animals* (3 rabbits, 4 white rats, 1 chicken, and 2 pigeons) the capillary walls in the mucosa of the intestinal tract were, here and there, black in color, especially distinct in the lower regions. The migratory cells were moderately filled with black pigments. In the epithelial cells, however, pigment was seldom found in any region. A catarrh or very slight hemorrhage was seen in the mucosa of all regions.

In three *very young rabbits* the findings were of a little different character. The coloring of the capillary walls and the phagocytosis of the migratory cells were only slight in degree, and the excreting pigment in the epithelium was found especially in the stomach and small intestine, even though slight.

4. *Arsenic Experiment.*—In *grown animals* (7 rabbits, 7 white rats, 1 dog, 3 chickens, and 3 pigeons), a hemorrhagic inflammation was noticed in the small intestine, especially distinct in the middle portions, and more or less catarrhal changes in the other regions of the intestine. Histologic examination showed degeneration, necrosis, and desquamation of the epithelial cells, with moderate hemorrhage and infiltration of round cells.

In four *very young* rabbits ranging from 4 to 9 days old, a diffuse catarrh in the intestinal tract, especially distinct in the stomach and small intestine, was in most cases produced. In the histologic examination, swelling and degeneration of the epithelium, hyperemia and very slight infiltration of round cells were found.

5. *Chromium Experiment.*—In *grown animals* (5 rabbits, 3 white rats, 2 dogs, 5 chickens, and 2 pigeons) a catarrhal inflammation was produced which extended from the lower regions to the small intestine. In the case of dogs, erosions and partly necrotic inflammations were found in the large intestine, but these were slighter than in the case of mercury poisoning. Histologic examination showed degeneration, necrosis, and some desquamation of the epithelial cells, with infiltration of round cells, and slight hemorrhage, except in cases of necrotic inflammation.

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[2] Heilborn: Arch. f. exper. Path. u. Pharmakol., 1878, **8.**

[3] Kaufmann: Virchow's Arch. f. path. Anat., 1889, **117,** 227.

[4] Virchow: Deutsch. med. Wchnschr., 1887, p. 1047.

In *very young animals* (five rabbits ranging from 4 to 18 days old, and a dog a few days old) a diffuse catarrh was found, especially distinct in the stomach and small intestine, and sometimes accompanied with miliary hemorrhages and erosions. Histologic examination showed a diffuse swelling and degeneration of the epithelium, edema, slight hemorrhage, and very slight infiltration of round cells.

6. *Cantharides Experiment.*—In *grown animals* (5 rabbits, 4 white rats, 1 dog, 3 chickens, and 2 pigeons), a catarrhal enteritis was produced which was most intensive in the small intestine, and was distinguished by its desquamative nature. Histologic examination showed a diffuse swelling, degeneration, necrosis and intensive desquamation of the epithelial cells, together with intensive exudation and infiltration of round cells; but hemorrhages were rare and slight.

In three *very young rabbits* ranging from 3 to 9 days old, and a dog a few days old, a diffuse catarrh was found in all regions, especially intense in the stomach and small intestine. Histologic examination showed a diffuse retrogressive alteration of the epithelium, edema, and a very sight infiltration in the membrana propria and submucosa.

7. *Ricin Experiment.*—In *grown animals* (9 rabbits, 1 dog, 7 white rats, 6 chickens, and 3 pigeons) were found catarrhal inflammation in the first stage, hemorrhagic inflammation of Peyer's patches in the second stage, diffuse hemorrhagic inflammation in the small intestine in the third stage, especially distinct in rabbits and rats. In other regions of the intestine more or less catarrh was observed, and some hemorrhage. Histologic examination showed intensive hyperemia and hemorrhage, with infiltration of round cells in the mucosa of the small intestine. In the lymph nodes, especially in Peyer's patches, diffuse hemorrhage was found, associated with swelling, phagocytosis, and degeneration of the reticuloendothelial cells of the follicles. The epithelium of the mucosa was degenerated, necrosed, and desquamated.

In the case of *very young animals* (11 rabbits ranging from 3 to 30 days old, 3 dogs ranging from 2 to 30 days old, and 2 chickens 3 days old) a diffuse catarrh was produced, extending throughout all regions of the intestinal tract; sometimes more or less hemorrhage was found in various regions, but never distinctly located in the small intestine. Histologic examination showed slight infiltration and hemorrhage, with swelling or some degeneration of the epithelium.

In cases of rabbits 3 months old the findings were similar to those of grown animals.

Kusama[5] also wrote as the result of experiment that ricin produced a hemorrhagic inflammation in the intestinal mucosa.

8. *Snake Poison Experiment.*—Findings in *grown animals* (9 rabbits, 4 white rats, 2 dogs, 2 chickens, and 3 pigeons) showed catarrhal inflammation in the first stage, hemorrhagic inflammation in the second stage, and necrotic inflammation in the third stage in the stomach mucosa. Necrotic inflammation was especially located in the middle third of the larger curvature, *at the same place where metals such as bismuth and mercury were sometimes noticeably excreted.* In the convalescent stage the mucous membrane of this part became cicatrized. Catarrhal changes were also observed to some extent in other regions, gradually diminishing as one approached the lower portions of the intestinal tract.

Histologic examination in the first stage showed an intensive swelling and some degeneration of the epithelial cells in the mucosa of the stomach, together with a moderate hyperemia. In the second stage, a moderate hemorrhage was found, principally in the propria. In the third stage, a diffuse necrosis of the mucous membrane was observed, together with intensive hemorrhage and infiltration in the submucosa. And in the convalescent stage, an intensive proliferation of the connective tissue was produced, with retrogressive alteration of the epithelial cells. In other regions of the intestine a trace of the foregoing changes only was seen, but nowhere was necrotic inflammation found.

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[5] Kusama: Zieglers Beitr. z. path. Anat. u. z. Allg. Path., 1913, **55**, 459.

Findings in eight *very young rabbits* ranging from 4 to 9 days old showed a diffuse, intensive, catarrhal inflammation, especially in the stomach and small intestine, together with a slight hemorrhage and some erosions; necrotic inflammation was nowhere found. Histologic examination showed swelling, degeneration, some desquamation of the epithelium, hyperemia, and, rarely, a slight hemorrhage.

Two animals were fed starch paste, *that the content of the stomach might be analogous with that of grown animals,* but no new results were found.

9. *Dysentery Toxin Experiment.*—Findings in *grown animals* (10 rabbits, 4 white rats, 2 dogs, 3 chickens, and 3 pigeons): First stage, catarrhal inflammation; second stage, hemorrhagic inflammation; third stage, necrotic inflammation, and in later stages, a cicatrization in the cecum (especially of rabbits) and large intestine (especially of dogs). These results are similar to those of Flexner[6] and Doerr.[7] In rats and pigeons a hemorrhagic inflammation was observed also in part of the small intestine.

Histologic examination: In the earlier stages, the epithelial cells were swollen in the lower portions; their nuclei seemed vesicular, or they were degenerated, showing the figures of karyolysis, or they were necrotic and desquamated. The membrana propria and submucosa were intensely edematous, with an infiltration of round cells and some bleeding. The hemorrhage and infiltration were most intensive in the area of necrotic inflammation, often extending into the muscle strata. In the protracted course of the intoxication some proliferation of the connective tissue in the mucous membrane was seen. In the lymph follicles of the vermiform process was found a swelling, a degeneration, and at times a necrosis of the reticulo-endothelial cells.

Findings in *very young animals* (11 rabbits ranging from 3 to 30 days old, 3 dogs, ranging from a few days of age to 2 weeks, and 7 chickens ranging from 5 to 11 days old): In cases examined in less than three weeks after birth the most distinctive changes were catarrhal or hemorrhagic inflammation in the stomach and small intestine, with more or less bleeding in the lumen. Of course, in the cecum and large intestine certain slighter catarrhal changes and some erosions were found; nowhere was a typical necrotic dysenteric inflammation found.

Histologic examination: The epithelial cells were diffuse and moderately swollen; their cytoplasm became distinctly granular and often showed vacuolation; their nuclei were vesicular or showed some figures of karyolysis, and occasionally the epithelium was necrotic and desquamated, especially on the ends of the villi. In the section stained for fat, a moderately diffuse fatty degeneration of the epithelium was seen, not only near the ends of the villi, but often on the glandular parts. The membrana propria and submucosa were more or less edematous, with more or less hemorrhage and slight infiltration of round cells. These findings were especially distinct in the small intestine and stomach. Peyers patches were often swollen, lymph follicles were often proliferated in some degree, and sometimes there was bleeding.

In animals over 2 months of age the findings were similar to those in grown animals.

10. *Paratyphoid B Toxin Experiment.*—In *grown animals* (6 rabbits, 5 rats, a dog, 2 chickens, and a pigeon) catarrhal or hemorrhagic inflammation was produced, which was usually distinct in the cecum and large intestine and slight in the small intestine. In the last stage of the poisoning a necrotic inflammation was found in the cecum of rabbits and rats. In comparison with cases of dysentery toxemia, this necrotic inflammation was of a more localized character and of smaller area. Histologic examination showed that the necrosis

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6. Flexner: Jour. exper. Med., 1906, **8,** 514.
7. Doerr: Ergebn. d. allg. Path. u. path. Anat., 1912, **16,** 122.

of the mucous membrane was of a superficial character, but hemorrhage was moderately distinct. In the earlier stages the swelling and degeneration of the epithelial cells were found, with more or less infiltration of round cells.

The lymph follicles in the intestinal tract were more or less swollen. Histologic examination showed a moderate proliferation of the reticulo-endothelial cells in the follicles, especially distinct in the vermiform process and the ileocecal patch; necrosis of the proliferated cells was nowhere observed, as is found in the case of typhoid-toxin poisoning. The lymph cells, also sometimes were more or less proliferated.

In *very young animals* (3 rabbits ranging from 3 to 10 days old, a dog 5 days old, and 6 chickens ranging from 3 to 13 days old) catarrhal inflammation was chiefly found, together with slight hemorrhage, at times, in all regions, and especially distinct in the stomach and small intestine. Moderately diffuse swelling and degeneration of the epithelial cells, slight hemorrhage, and a slight emigration of round cells were seen histologically.

In the lymph follicles a proliferation of the lymph cells was seen in the foreground, while the reticulo-endothelial cells were not so distinctly proliferated.

An Experiment with Typhoid-Toxin.—In the case of a *grown rabbit,* which was poisoned with typhoid toxin, was observed an intensive proliferation and a diffuse necrosis of the reticulo-endothelial cells in the vermiform process and ileocecal patch—typical typhoid changes—while in two cases of *very young rabbits,* under the same conditions, no such typical typhoid changes were produced. In other regions of the intestine nothing more was seen than a catarrh of the mucosa.

From the foregoing findings we may conclude that the paratyphoid B toxin produces changes closely related to but slighter than those of experimental dysentery in the lower portions of the intestine, combined with changes nearly related to those of experimental typhoid in the lymph follicles of the intestine.

Pathologic-anatomic observations on paratyphoid B disease, as far as I know, has not been reported on extensively until recently. Huebschmann[8] wrote that this disease produced, in most cases, slight dysenteric changes in the large intestine, without typical typhoid changes anywhere. Ring[9] and Buday[10] have seen miliary ulcers in Peyer's patches and in the mucosa of the small intestine; Saltykow[11] has found typhoid changes in several cases and dysenteric changes in others.

From the findings of these men it is evident that the paratyphoid B disease should produce changes closely related to those of dysentery, combined with changes nearly related to those of typhoid, justifying the conclusion that the changes which result from experimental poisoning with paratyphoid B-toxin are caused by the excretion of this toxin into the intestinal tract.

11. *Cholera Toxin Experiment.*—In cases of *grown animals* (8 rabbits, 2 rats, a dog, 3 chickens, and 2 pigeons) catarrhal inflammation was chiefly found in the small intestine (together with some hemorrhage) distinguished especially

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[8] Huebschmann: Ziegler's Beitr. z. path. Anat. u. z. allg. Path., 1913, **56,** 514.

[9] Rings: Med. Klin., 1907, p. 1007.

[10] Buday: Centralbl. f. Bact., Part 1, Orgl., 1911, **60,** 449.

[11] Saltykow: Virchows Arch. f. path. Anat., 1913, **211,** 467.

by its desquamative nature. Histologic examination distinctly showed desquamation of the superficial epithelium and a moderate swelling of the deep epithelium, and also a moderate infiltration of round cells.

In cases of *very young animals* (3 rabbits ranging from 3 to 5 days old and 5 chickens from 3 to 30 days old) the changes in the stomach mucous membrane were also distinct, so that the stomach contents were often mixed with blood, and in the stomach and small intestine the alteration of the epithelial cells was diffuse, while the infiltration of round cells was always very slight.

CONCLUSION AND DISCUSSION

1. *Excretion of Poisons in the Gastro-Intestinal Tract.*—The mucous membrane of the gastro-intestinal tract of the animals poisoned by the injection of the poisons mentioned usually showed certain changes. These changes were not of the same degree in all regions, but acted most violently on a certain region; for example, on the stomach, small intestine, cecum or large intestine, depending on the kind of poison used; even though some differences were found, these were caused by the varied forms of intestinal tracts, or by the peculiar predisposition of different animals.

A problem arises, How far does the chemical action of the intestinal content (combined with excreted poisons) influence these principal changes of the intestine? No definite answer can be determined by experimental findings, but I shall state several important facts concerning this problem.

The principal change in grown animals caused by bismuth and mercury was most distinct in the cecum of rabbits; in the case of rats it was moderately localized to about the middle portion on the side toward the mesenteric fixation of the cecum; while in dogs it was most distinct in the large intestine.

The dysenteric changes in the case of rats usually extend to the middle portions of the small intestine, while it was chiefly localized in the cecum of rabbits and in the large intestine of dogs.

In the mucosa of the vermiform process of rabbits, no such characteristic changes were produced as in the mucosa of the cecum, when poisoned with bismuth, mercury, dysentery, and paratyphoid B toxins.

The changes in the small intestine in most cases were most distinct in the middle portions.

The changes in the stomach were localized to a certain part of the fundus.

From these facts we may conclude that the poisons injected were excreted most distinctly in certain regions of the intestinal tract, and this was fundamentally responsible for the specific localization of the principal changes in the intestine, even though the chemical action of the intestinal content might take a part in causing the formation of these changes.

From the data obtained we can divide the poisons into five groups according to the principal region of their excretion in the intestinal tract.

Group 1. Poisons which are most distinctly excreted in the stomach mucosa; for example, snake poison.

Group 2. Poisons which are most distinctly excreted in the small intestine; for example, arsenic, ricin, cantharidin and cholera toxin.

Group 3. Poisons which are most distinctly excreted in the lower portions (the cecum and large intestine); for example, bismuth, mercury and dysentery toxin.

Group 4. Poisons which are most distinctly excreted in the lower regions, with a noticeable excretion in the small intestine; for example, chromium and paratyphoid B toxin.

Group 5. Poisons which are not distinctly excreted in any region of the intestine; for example, silver.

The excretion of poisons by the mucous membrane of the gastro-intestinal tract seems to arise in three ways: (1) secretion by epithelial cells; (2) phagocytosis of the migratory cells; (3) phagocytosis of the reticulo-endothelial cells in the lymph follicles of the intestine.

These phenomena were recognized microscopically in cases of bismuth tested animals. In other cases, also, we noticed an alteration of the epithelium, an activity of migratory cells, and a swelling of reticulo-endothelial cells. In most cases, however, excretion by the epithelium appears to be the most important factor.

2. *Enteritis by Excretion.*—Enteritis by excretion, as I will call it, is an inflammation of the mucous membrane produced by the excretion of poisonous substances into the intestinal tract. The anatomic and histologic changes of this enteritis depend on the quality of the poisons. Enteritis by excretion of mercury, which has an intensively corrosive effect, is of a hemorrhagic and necrotic character; while the enteritis by excretion of bismuth, which has a milder effect, usually shows no such intensely destructive tendency. The dysentery toxin produces a necrotic affection in the lower regions of the intestine, while the excretion of the cholera toxin results in a desquamative catarrh of the small intestine.

Or, we may say that the changes of this enteritis depend on whether the excreting poison affects most intensively the epithelium, the vessels, or the connective tissue.

From data obtained we may divide poisons into three groups, according to the nature of enteritis produced by their excretion in the intestinal tract:

1. Catarrhal poisons: silver, bismuth, chromium, cantharidin and cholera toxin.
2. Hemorrhagic poisons: arsenic and ricin.
3. Necrotic poisons: mercury, snake poison, paratyphoid B, and dysentery toxin.

Of course, the catarrhal poisons may result in more or less hemorrhage, as in like manner, hemorrhagic poisons may produce, secondarily, partial necrosis, as in the first stage of poisoning by hemorrhagic or necrotic poisons we only observed a catarrh. Therefore, the changes of this enteritis also depend on the doses used and the stage of the poisoning. Moreover, the animals may show a peculiar predisposition, in some degree, toward each poison.

In all stages of poisoning, however, this enteritis showed a character which was specific to a certain degree for each kind of poison, but it was especially specific in the principal region of intestinal excretion.

In the histologic examination of this enteritis there were two factors noteworthy, namely, a destructive process and a reactive process, especially distinct in the principal regions of intestinal excretion. The reason why a poison elects a certain region of intestinal excretion, is not clearly explained. It is interesting that the principal changes found in experimental enteritis by excretion of dysentery, paratyphoid B, typhoid and cholera toxins are similar to those which we usually find in necropsies after dysentery, paratyphoid B, typhoid, and cholera. Therefore, each of these bacterial toxins will find a principal region for intestinal excretion, which region is the place of predilection of these bacterial infections. Hence, we may say that every poison will have the greatest affinity for its principal region of intestinal excretion.

3. *Compensational Excretion in the Intestinal Tract.*—In several groups of chickens and rats the cecum was extirpated; then the animals were poisoned with bismuth and mercury. The most distinctive changes were observed in the large intestine and in the middle portions of the small intestine. In the cases of pigeons, which anatomically have the most rudimentary cecum, the most intensive changes were usually produced in the large intestine and in part of the last loop of the small intestine, when they were poisoned with bismuth, mercury, and dysentery toxin. These changes in the small intestine must be due to the result of a compensational excretion of poisons.

Also, in cases of most acute poisoning of grown animals by all the poisons used in our experiments, the changes produced were found to be, to a certain degree, of a more diffuse character than in cases of subacute poisonings. This result must be also due to a compensational excretion in all regions of the intestinal tract, and it was more or less closely related to the general findings of very young animals.

4. *Excretion of Poisons in the Intestinal Tract of Very Young Animals.*—The method of excretion of bismuth injected in very young animals was so characteristic that the excreted bismuth granules were found microscopically to be moderately diffused throughout all the intestinal tract; and not alone in the surface epithelium, but also in the deep epithelium; while in the case of grown animals the metal was

excreted, principally and in more concentrated form, from the epithelium on the ends of the villi in the cecum and large intestine.

In all stages of experimental poisoning with mercury, ricin, snake poison, dysentery and paratyphoid B toxins, the intestinal mucosa of the very young animals showed neither typical necrotic nor typical hemorrhagic inflammation in the described region, as is usually the case in grown animals, but an enteritis of a diffuse, and, in most cases, of a catarrhal nature.

By histologic examination a diffuse epithelial alteration (swelling and degeneration showing the figures of karyolysis, and often a diffuse fatty degeneration) was always found; a slight hemorrhage might also be found here and there, while the reactive infiltration of the round cells in the mucous membrane was usually very slight. In the lymph follicles of the intestinal tract, however, was often seen a swelling, especially in cases with bacterial toxins, and a proliferation of lymph cells.

From data obtained in regard to the excretion of poisons in the intestinal tract of very young animals, three characteristics are revealed:

1. The excretion takes place diffusely and is consequently thinned.
2. The enteritis by excretion is anatomically of a diffuse character and less specific to every poison offered.
3. The destructive process is relatively distinct in regard to the histologic findings, showing a diffuse epithelial alteration, while the reactive process is slighter in comparison with findings in grown animals.

The imperfect development of the tissue and the imperfect differentiation in the function of the mucosa ought to be responsible for these characteristics.

There are several reasons to support this opinion. From an anatomic standpoint, the intestinal tract of very young normal animals offers something of especial interest. The important points are that the formation of the glands in the intestinal mucosa is not yet perfected and the mucosa is poorer in connective tissue and wandering cells, while it is richer in vessels, in comparison with that of grown animals.

In cases of young animals ranging from 3 weeks (at which time the animals usually begin to take some food besides milk from the mother animals) to about 2 months of age, the physiologic structure of the intestinal mucosa gradually approaches that of grown animals; in like manner, I often saw, in experimenting with young animals of these ages, that the enteritis produced gradually approaches the findings in grown animals.

5. *Comparative Observations of the Pathologic-Anatomic Lesions of Enteritis in Infants with Enteritis by Excretion in Very Young Animals.*—In most cases of nutritional disturbance or infectious enteritis of infants the pathologic-anatomic lesions are of a diffuse nature

in all regions of the intestinal tract, often particularly distinguished by diffuse alterations of the epithelial cells.

Infectious diseases of the intestine of infants, such as dysentery and typhoid, often have atypical clinical signs, and pathologic-anatomic lesions often appear less severe in degree than in adults, but with atypical localization, inclined to be of a diffuse nature.

The foregoing characteristics in infants are closely related to the figures found in the enteritis by excretion of very young animals, and must be due to the imperfection of the development and function of the intestinal mucosa.

In regard to the imperfect development of the tissue of the intestinal tract in infants, there are statements by Baginsky[12] and Gundobin.[13] I have examined the intestines of several infants and about forty infants dead of enteritis. The results will be made known in the future.

By the same method of reasoning it may also be explained that the so-called "enteritis by parenteral infection," which may be an enteritis by excretion, usually causes much severer disturbances in infants than in adults.

The swelling and proliferation of the lymph follicles which are often seen in nutritional disturbances or enteritis in infants, may be caused, to a certain degree, by poisonous substances produced in the intestine, according to the results of my experiments. This view is in accordance with that of Finkelstein.[14]

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[12] Baginsky: Virchows Arch. f. path. Anat., 1882, **89,** 64.

[13] Gundobin: Die besonderheiten des Kindesalters, 1912, pp. 263 and 303.

[14] Finkelstein: Lehrbuch der Sauglingskrankheiten, 1912, **3.**

A NEW APPARATUS FOR PUNCTURE OF THE SUPERIOR LONGITUDINAL SINUS *

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The value of the superior longitudinal sinus as a route for venipuncture for therapeutic and diagnostic purposes in young infants has recently been established. This procedure is now generally accepted as safe and practical. Tobler[1] was the first to study the anatomic relations of the sinus for the purpose of using it as means of obtaining blood and administering fluids. He showed that the puncture is best made in the midline at the posterior angle of the fontanel, where the sinus has its greatest depth. Tobler's measurements show that the distance from the skin to the lumen of the vein is from 2 to 5 mm., according to age and individual variations, and that the depth of the sinus at the posterior angle of the fontanel varies from 4 to 7 mm.

While sinus punctures are now made in practically every hospital for infants whenever venipuncture is necessary, a suitable apparatus combining the advantages of simplicity, cheapness and easy applicability has not been described. Helmholz[2] has devised an apparatus for direct transfusion into the sinus. It is a combination of the Unger apparatus with a device which steadies the baby's head and supports an ordinary needle introduced obliquely into the posterior angle of the fontanel. The apparatus has to be attached to an operating table and is rather complicated and cumbersome. The needle is introduced through a guide fastened to the child's head by adhesive plaster and set at a definite angle with the scalp. No provision is made, however, for guarding against penetration of the dura, as the needle is fastened in place only after the puncture is made.

Brown and Smith[3] used an ordinary needle, with a short bevel, on which was mounted a ridge of solder about 2 mm. thick, a quarter of an inch from the tip of the needle. This did not allow for adjustability. Several needles with various lengths beyond the guard would have to be kept on hand, which, through repeated sharpening, would soon become too short for use. Furthermore, the needle is difficult to keep steady when held between the thumb and forefinger against the child's head.

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* Submitted for publication Aug. 15, 1918.

* From the Babies' Hospital.

1. Tobler: Monatschr. f. Kinderh., 1915, **13,** 384.
2. Helmholz, H. F.: Am. Jour. Dis. Child., 1915, **10,** 194.
3. Brown, A., and Smith, G. E.: Am. Jour. Dis. Child., 1917, **13,** 501.

A simple apparatus has been devised by the writer which we have been using in the wards of the Babies' Hospital with satisfaction. It is adjustable to any desired length; it can be held securely in place despite movements of the infant's head, and it provides against puncture of the dura or injury to the brain cortex.

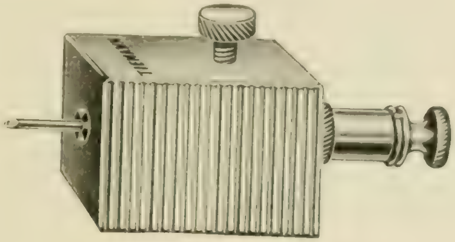

Fig. 1.—Author's apparatus.

The apparatus consists of an 18-gage needle with an obturator, a cylindrical sleeve and an aluminum block (Fig. 1). The barrel of the needle is 4 cm. long and has a bevel of 45 degrees. The hub is threaded and made to screw into the cylinder, which is 3 cm. long and 4 mm. in diameter, thus allowing 1 cm. of free needle to project beyond it. The cylinder with its contained needle fits into a bore through the middle of the aluminum block. The latter carries a set screw which secures the cylinder, setting the needle at any desired length beyond the block. A gage on the cylinder indicates the number of millimeters which the needle projects. Two opposite sides of the block are corrugated in order to insure a firm hold.

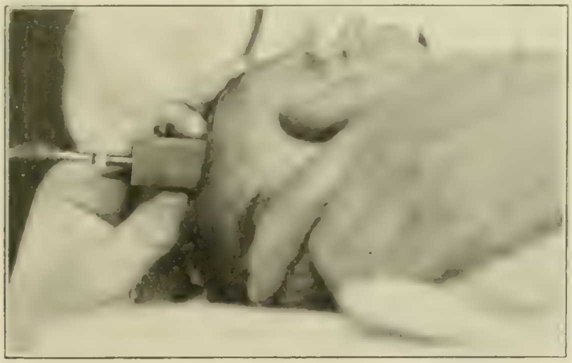

Fig. 2.—Method of using apparatus.

On examining Tobler's measurements, it will be seen that the distance from the skin to the apex of the sinus at the posterior angle of the fontanel will vary from 6 to 12 mm. in infants of different ages. It would seem, then, from these figures, that inserting the needle to the depth of 4 mm. in a young infant and 6 mm. in an older one, would bring the needle well within the lumen of the sinus without the slightest danger of either injuring its walls or penetrating beyond them into the subdural space. In our experience we have found this to be the case.

The needle is adjusted at the desired distance and secured by the set screw. The sinus is entered at the posterior angle of the anterior fontanel at right angles to the long axis of the skull. When the needle is in place in the sinus the aluminum block rests against the child's head and prevents movements of the needle in any direction (Fig. 2). The crying of the infant raises the pressure in the sinus, so that when the obturator is removed the blood begins to flow. A syringe or gravity apparatus, as the case may be, is quickly attached to the hub and the procedure carried out in the usual manner. It is not necessary to replace the obturator before removing the needle. The reason for making the apparatus with an obturator is to obviate the occasional possibility of blocking the needle during its passage through the skin. This has occurred with us on two occasions while using an ordinary needle for sinus puncture.

The apparatus can be manufactured at a small cost; it is extremely simple, compact and easily manipulated; and it can be employed without any of the dangers or disadvantages presented by the use of ordinary needles in this work.

135 East Fifty-Fifth Street.

TERTIAN MALARIA IN TWO INFANTS UNDER TWO MONTHS OF AGE *

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It is not unusual for practitioners in our section to see malaria in its various expressions among children and adults, but it is unusual to note this particular malady in infants under 6 months of age. Medical literature has not given us many references concerning the signs and symptoms referable to malaria in the very young, and the writer presents these two cases in the belief that the manifestations expressed in these cases may be of sufficient interest to justify their publication.

Case 1.—Lillian P., aged 2 months, was brought to me on account of fever. She was an only child. Her father is living and healthy, but her mother died at the time of her birth from puerperal fever. Her feeding history has been a most irregular one, several of the proprietary foods having been given with but little success. At the time of admission a condensed milk formula was being given. She was admitted to Touro Infirmary, July 15, 1918.

Physical Examination.—A frail infant, poorly nourished and developed, possessing marked cachexia. The mucous membranes were extremely pale and the musculature flabby. She apparently was very listless and did not respond as would the usual child when a physical examination is made. Her reflexes were remarkably diminished. The findings in the chest and abdomen were negative, the exception being that the spleen was markedly enlarged, the lower border approaching the upper border of the pelvis. On palpation the spleen was moderately hard and not particularly of the type one would expect in malaria.

Laboratory Findings.—Urine, negative; stools, constipated movements, well digested; smear (vaginal), negative; blood, hemoglobin, 25 per cent.; total red count, 2,000,000; total white count, 15,000; tertian plasmodium found in large numbers.

Treatment.—Quinin was given at intervals of two hours, 0.4 grain, in three doses, the last dose being given two hours before the expected rise in temperature. The infant was discharged from the hospital, July 22, and up to this writing has had no recurrence of temperature elevation and has made a steady gain in weight.

Case 2.—Aug. 6, 1918, a female child was admitted to the Touro Infirmary on account of continued fever which she had had for four weeks. The temperature did not respond to the usual medication and the physician was at a loss to account for this prolonged elevation of temperature.

Physical Examination.—A desperately sick infant, appearing in a state of profound stupor; aged 7 weeks; marked cachexia; mucous membranes extremely pale; the musculature lacked tonicity and from the appearance of the skin this baby undoubtedly had lost in weight. Other than a murmur elicited from the base of the heart and a typical malarial spleen, much larger than in the first case, the infant did not present any clinical manifestations that would be of service in making a diagnosis.

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* Submitted for publication Aug. 21, 1918.

Laboratory Findings.—Blood: hemoglobin, 25 per cent.; total red count, 2,600,000; total white count, 13,750; tertian malarial plasmodium found in large numbers; vaginal smear, negative.

Treatment.—After having been treated for five days, the infant was discharged from the hospital and up to the present report had not had a recurrence of temperature elevation. It is interesting to note that the tertian plasmodium was recovered from the mother and that she gave a history of *having had malaria prior to the birth of her child.*

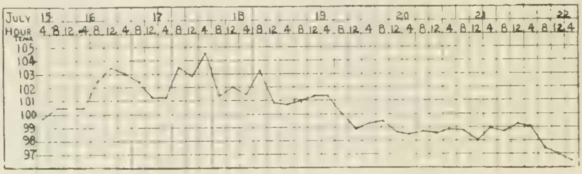

Fig. 1.—Temperature Curve in Case 1.

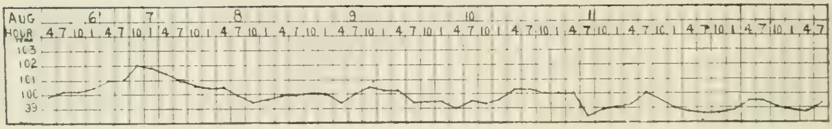

Fig. 2.—Temperature Curve in Case 2.

SUMMARY AND CONCLUSIONS

1. Tertian malaria, although uncommon in infants, does occur.

2. The common symptoms noted are: (*a*) Marked cachexia; (*b*) a corresponding marked diminution in hemoglobin and in the red blood cell count; (*c*) enlarged spleen; (*d*) prolonged temperature (atypical as compared with adults).

3. A soluble preparation of quinin, 0.4 of a grain, in three doses, was given for seven consecutive days and thereafter every other day for one month.

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PROGRESS IN PEDIATRICS

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF CHILDHOOD *

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(Continued from November Number)

EMBRYOLOGY AND ANATOMY

Anomalies and Malformations.—In a recent paper by the late Prof. Franklin P. Mall[63] it is calculated that the ratio of abortions to full-term births is about 1 to 4. And also that the frequency of localized anomalies in abortions is 7.5 per cent.; and that localized anomalies should be noted about twelve times as frequently as full term monsters. Studies seem to justify the conclusion that "pathologic embryos, as well as those which are normal in form, are very frequently associated with localized anomalies and that abortion usually follows as a result of serious lesions in the chorion, as well as in its environment. Should the alterations in the embryo and in the chorion be very slight, and the condition of the uterine mucous membrane, which may be expressed by the term inflammation, be overcome, the pregnancy in all probability would go to term and end in the birth of a monster or an infant presenting well recognized malformation."

Poisons produced by an inflamed uterus cannot be viewed as the sole cause, since pathologic ova occur far more commonly in tubal than in uterine pregnancy. Conditions of implantation may be a factor. Whether in the end all malformations are brought about by some simple mechanism, as alteration in the amount of oxygen or some other gas, remains to be demonstrated. It is perfectly clear that monsters are not due to germinal and hereditary causes, but are produced from normal embryos by influences which are to be sought in their environment. It may not be very far amiss to attribute these conditions to alterations in the nutrition of the embryo. Disorganization may occur, accompanied at first by cytolysis, and, as it progresses more rapidly, by histolysis, the two processes not acting with equal severity on all parts of the embryo. "When we consider the whole ovum, it is the embryo itself which is first destroyed; while within the embryo the central nervous system or the heart is the portion which is first affected."

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[63] Mall, F. P.: Frequency of Localized Anomalies in Human Embryos and Infants at Birth. Am. Jour. Anat., 1917, **22,** 49.

In discussing the origin of merosomatous monsters, hardly more has been stated by most authors than that there has been an arrest of development, but Mall has attempted to point out that the primary cause is in the environment of the egg, and that the arrested development is associated with the destruction of tissue. It is inconceivable to him that cyclopia should begin in an embryo after the eyes are once started in normal development; or hare-lip after the upper jaw has once been well formed; and this view is extended to include clubfoot, spina bifida occulta, and other types of malformation.

Comby[64] has recently reviewed the subject of phocomelus deformity, a monster in which the hands and feet appear to be inserted immediately on the trunk, as in the seal. A number of subdivisions of the condition are recognized, and a case recently described by Mlle. Hélène Socin is given in some detail.

A. Silva Filho[65] reports the presence of a parasitic heterodelphus monster in a young child.

C. Fino[66] records the occurrence of a double monster united by the sternum. An instance of ischiopagus twins is reported by W. Salmond.[67]

Watt[68] describes with much detail a 7 months fetus that exhibited the rare deformity of complete absence of the ulna in each arm, accompanied by the still much rarer condition of monodactyly. Careful dissection of the cutaneous distribution of the median nerve in the hand of the monodactylous fetus led to the conclusion that the single finger present represented the second digit, and militated against the hypothesis that it resulted from fusion of five digits. Roentgenograms of the right and left arm are presented.

P. Lewis[69] discusses congenital absence or defects of the bones of the extremities.

Abt[70] reports a case of congenital skin defect. The baby was normal in weight and size and had been born in normal labor. It presented a defective skin area over each knee. These areas were about 1 by 1¼ inches in size, almost identical in size and shape, and seemed to be, so to speak, irregularly punched out. The base was beefy red and moist, and a few small foci in this red ulcerated surface showed a yellow exudate; there were indications of beginning cicatrization. These areas gradually covered over so that after five or six weeks the denuded red areas were replaced by shining, white patches, somewhat lighter in color than the surrounding skin. The healing process was complete and the baby appeared normal in every respect.

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[64] Comby, J.: Phocomelous Deformity. Arch. de méd. d. enf., 1918, **21,** 33.

[65] Filho, A. Silva: Heteradelphus Parasitic Monster on Young Child. Rev. med. cirug., Brazil, 1918, **26,** 30.

[66] Fino, C.: Sternopagus Double Monster. Gazz. d. osp., 1917, **38,** 875.

[67] Salmond, W.: Case of Ischiopagous Twins. Lancet, London, 1918, **1,** 295.

[68] Watt, J. C.: Anatomy of a Seven Months' Fetus Exhibiting Bilateral Absence of the Ulna, Accompanied by Monodactyly (and also Diaphragmatic Hernia). Am. Jour. Anat., 1917, **22,** 385.

[69] Lewis, P.: Congenital Absence or Defects of Bones of the Extremities. Am. Jour. Roentgenol., 1917, **4,** 431.

[70] Abt, I. A.: Congenital Skin Defects. Am. Jour. Dis. Child., 1917, **14,** 113.

The so-called congenital skin defects have not been recorded frequently. The majority of accessible reports deal with skin defects of the scalp. They are usually circular in shape, sometimes oval or irregular, generally have clear-cut edges, and vary in size from a pinpoint upward. The first authentic case appears to have been reported by an English physician, Campbell, in 1826. Priestley reported one in 1859. Emanuel, in 1915, reported an infant with congenital absence of skin involving hands, legs, and feet. The child was stillborn; there was no evidence of syphilis.

The lesions are generally attributed to "errors in development or to inflammatory adhesions between the external layers of the skin and the amnion. At the point where the adhesion has taken place, the growth of flat epithelium is retarded." Other congenital malformations such as deficient fingers, hands, or feet, are not infrequently associated with congenital skin defects. Abt's report is accompanied by a tabulation of reported cases, by illustrations of certain of them, and by a colored plate showing the local appearance in his own case.

Litchfield[71] reports a case of "harlequin fetus." When born the child was incased from head to foot in a greatly thickened epidermis, which was cracked and seamed in many directions, but chiefly at the natural folds and wrinkles of the surface. The material formed thick, hard plates of skin, the edges of which were curling up. The natural elasticity of the skin was nowhere apparent. With careful nursing, cleanliness and anointing of the skin with white petrolatum and lanolin, the child has reached 8 years of age in a fair state of health, and is mentally bright. Her condition is one of severe ichthyosis.

Weber[72] writes on the subject of congenital hirsutes in the child.

Herbert Thoms[73] reports an instance of family prevalence of anencephaly. Ballantyne, in his series of 325 cases of monstrosity and fetal disease, noted forty-six anencephalics, an incidence of 14 per cent. In only two of the series had the mother previously given birth to an anencephalic fetus. Other instances have been noted by Lammert,

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[71] Litchfield, W. F.: A Case of Harlequin Fetus. Med. Jour. Australia, 1918, **1,** 494.

[72] Weber, F. P.: Congenital Hirsutes in a Child. Brit. Jour. Child. Dis., 1917, **14,** 272.

[73] Thoms, Herbert: Report of a Case of Family Prevalence in Anencephaly. Jour. Am. Med. Assn., 1918, **70,** 10.

Carli, and Martin. The fetus, if born alive, usually dies quickly, though Ross reported a case in which the child lived more than sixteen days. In the instances reported by Thoms, both fetuses were stillbirths. The pregnancies were not otherwise abnormal, and the Wassermann test, paternal and maternal blood, was negative, as was the microscopic examination of the placenta.

The second fetus weighed 2,150 gm. and was 48 cm. in length. It presented a typical picture of anencephaly with complete spina bifida. The head presented the well known appearance, the cranial vault and the scalp being practically absent, and this portion of the head was covered by thickened dura mater, which was dark red. The head was deeply set on the shoulders, the eyelids protruding and thickened, the forehead absent, the nose flattened, the mouth open, and the tongue protruding. The whole cerebrospinal canal from end to end was open. The vertebral arches in no place were united posteriorly, and were separated from 3 to 4 cm. most of the distance. The entire canal was covered by dura mater through which a few strands of nervous tissue could be seen. The remainder of the body was that of a well formed male child.

An instance of congenital enophthalmos is described by Lutz.[74] It appears that there have been very few publications on congenital defects of the motility of the eye. Birch-Hirschfeld (Monograph, 1917) found only 50 cases in the literature. The present article is well illustrated by photographs that show a small right eye not deflected to the right past the center line, and retracted, with diminution of the palpebral fissure in looking to the left.

McNaught[75] reports an instance of congenital occlusion of the right choana. The patient was an adult and the obstruction consisted ot a long wall extending from the floor to the sphenoid, and from the posterior end of the vomer to the lateral wall. After an adequate opening had been made in the wall, it was found by testing the sense of smell with some of the essential oils that the patient could detect the odor at once on inhalation; apparently the olfactory nerves were developed.

Congenital occlusion of the choanae of the nose has been recognized since 1830, when the condition was seen postmortem by Otto. Emmert (1854) first reported the condition in the living. About one hundred cases have been reported. Cases of supposed asphyxia neonatorum may have this as a cause; such a case was reported by Richardson in 1914. The causative factor is some departure from normal embryologic development.

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[74] Lutz, A.: A Case of Congenital Exophthalmos in Connection with Complete Absence of Abduction and Retraction of the Eyeball in Adduction. Arch. Ophth., 1917, **46**, 243.

[75] McNaught, H. Y.: Congenital Occlusion of the Choanae of the Nose. California State Jour. Med., 1918, **16**, 193.

Noxon Toomey[76] reports a case of congenital paramedian sinuses of the lower lip in which he summarizes the literature of the subject because its complete bibliography has heretofore been lacking in English literature.

The anomaly appears first to have been reported, in 1845, by Demarquay, who found ten cases in three families. The anomaly is usually associated with hare-lip and the lesion may consist of one or more slits leading into small saccules on the inner aspect of the lip. The sinuses may secrete mucus, particularly at meal times. Steda reviewed the literature on the subject in 1906, made a microscopic study of the lesion and concluded that the malformation arose from excessive growth through closure on both sides of the embryonal furrow of the lower lip, that is, through transformation of the lateral furrows into one canal. Huber, the histologist, arrived independently at a similar explanation. Regnier, 1913, has recently considered the subject in a monograph. Occasionally no other anomaly is present.

Toomey's case occurred in an eight months' old female infant. The baby had a complete cleft of the hard and soft palate; conditions that were successfully operated on. The more unusual anomaly is described as follows:

> Three millimeters on each side of median line of the lip and 6 mm. orally from mucocutaneous border is a sinus. The sinus mouths are not raised or inflamed and they admit nothing wider than the smallest Bowman probe. The sinuses point toward the chin and are 5 mm. deep. When squeezed they give vent to a small drop of clear mucus. Immediately orally from the mouth of each sinus is a white semilunar raised area, the cusps of which point anteriorly. Just in front of the sinus openings are hemispherically raised areas about 4 mm. in diameter.

Hughes[77] reports a case of congenital angioma of the tongue. It was seen at birth as a small swelling on the dorsum of the tongue and was diagnosed by the physician as a "birthmark." At the age of 16 years, the tumor had become as large as a marble and caused difficulty in mastication, and consequent indigestion. This condition became chronic. At the age of 26 years, the growth was the size of a large marble, reddish blue in color, well defined, with raised edges and smooth to the touch. No pain had ever been caused by it, and there had been no ulceration or hemorrhage from the growth. On pressure the growth could be reduced, but immediately filled up again when the pressure was removed. As the growth was a cavernous type of angioma, and benign, and the symptoms caused by it would be relieved by care and attention to the diet, it was felt best to treat the condition medically.

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[76] Toomey, Noxon: Congenital Paramedian Sinuses of Lower Lip. Arch. Pediat., 1917, **34,** 924.

[77] Hughes, F. M.: A Case of Congenital Angioma of the Tongue. Lancet, London, 1917, **2,** 749.

A case of cystic lymphangioma in the new-born is reported by R. McPherson.[78]

Ellis[79] reports a case of congenital absence of the left lung in an 8-year-old boy. The patient was of good development, but poorly nourished. He came to the hospital with a history of one week's illness, with chills and fever, and complained of pain in his knee. He died two weeks later with the following clinical diagnosis: Acute articular rheumatism; acute endocarditis; pericarditis with effusion; pleurisy with effusion.

At necropsy the left lung was found to be absent. The right lung extended well beyond the left costrochondral line and the large pericardial sac, containing 75 c.c. of fluid, occupied the remainder of the left side of the thorax. The left branch of the pulmonary artery and the left pulmonary veins were lacking. Two veins from the right lung entered the left auricle. The right lung was large, and roughly speaking, had the semblance of five lobes. The heart, other than large vegetations in the mitral leaflets, showed no noteworthy abnormality.

Complete absence of one lung is a rare condition. Ellis finds references in the literature to but eighteen of what appear to be certain cases. These he tabulates. There are five others that may be classified as possible cases.

Of the nineteen cases of absence of one lung, thirteen were of the left and six of the right. Interference with the blood supply in early embryonic life is supposed to be the cause in all cases.

Harmer[80] notes that according to Berger's teaching the brain inclusion in an encephalocele is abnormal brain tissue, cephaloma, nonfunctionating and insensitive. Harmer amputated it in four cases, three with the knife, and once with the cautery, apparently without ill effect. The four patients recovered. The thirty-four cases comprise seven meningoceles, twenty-three myelomeningoceles, three hydroencephaloceles, and one encephalocele. The total mortality was 47 per cent.

A. P. C. Ashurst[81] reports cases of birth injuries of the shoulder.

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[78] McPherson, R.: A Case of Lymphangioma in the New-Born. Bull. Lying-in Hosp., 1917, **11,** 165.

[79] Ellis, A. G.: Congenital Absence of Lung; Report of Case. Am. Jour. Med. Sc., 1917, **154,** 33.

[80] Harmer, T. W.: Spina Bifida and Allied Malformations—Thirty-Four Cases. Boston Med. and Surg. Jour., 1917, **177,** 353.

[81] Ashurst, A. P. C.: Ann. Surg.; 1918, **67,** 25.

Prince[82] reports the removal of a large cystic tumor of the uterus from a 11-hour-old baby girl. The infant presented a large hernia through which the large and small intestine could be clearly seen. There was decided lack of development of the left rectus muscle, and underneath could be felt a large tumor. This was at first thought to be a hydronephrotic kidney. At operation it was found to be a cystic tumor arising from the uterus. The left tube and ovary were missing. The endometrium appeared normal. After drainage of the cystic accumulation and replacement of the intestines the infant made an uninterrupted recovery. The writer argues for early operation on remediable congenital defects.

Novak,[83] in reporting six cases of congenital absence of uterus and vagina, states that according to Burrage the first instance of this condition was described in 1572 by Realdus Columbus. Since that time several hundred cases have been reported in the literature, most of the reports, however, being very brief, usually incomplete, and sometimes leaving doubt as to the correctness of the diagnosis. Absence of the vagina is usually associated with absence of the uterus. In the absence of menstruation, these patients may complain of definite molimina, nose bleed, or, more rarely, bloody discharge from the bowel may occur. Other anomalies may be associated, misplaced kidney being an important one. The patients all complain of nonappearance of the menstrual flow.

Bruce[84] reports delivering a multipara of an apparently normal male infant which next day presented a distended and tender abdomen and vomited bile. The child was then found to be discharging meconium through the scrotum. An opening was made into the rectum and dilated; meconium escaped. The opening was kept patent and the vomiting ceased. A month later the child was the picture of health; both orfices were open and he appearently had control over discharges at both openings. A probe when inserted through the scrotal opening passed backward and downward into the rectum.

A case of congenital umbilical hernia, ectopia vesicae and imperforate anus, is reported by F. C. Pybus.[85]

Determination of Age of Fetus.—Many reasons, purely scientific and other, make the determination of the age of the fetus of considerable practical importance. When the date of the last menstruation or the date of a single isolated coitus is not known, estimation of the age of the fetus has usually been made on the basis of the length of the fetus. All these methods are subject to considerable error. There are many physiologic and pathologic variations and numerous factors influence the length, the weight and also the measurement of the fetus. Additional or corroborative evidence from any source is desirable.

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[82] Prince, E. M.: Anatomic Defects in the New-Born Demanding Surgical Operation; Report of a Case of Uterine Tumor. Jour. Am. Med. Assn., 1918, **70,** 1212.

[83] Novak, E.: Congenital Absence of Uterus and Vagina; Report of Six Cases. Surg., Gyn. and Obst., 1917, **25,** 532.

[84] Bruce, J. R.: Case of Congenital Scrotal Anus. Jour. Missouri Med. Assn., 1918, **15,** 90.

[85] Pybus, F. C.: Case of Congenital Umbilical Hernia, Ectopia Vesicae, and Imperforate Anus. Brit. Jour. Child. Dis., 1917, **14,** 274.

Julius H. Hess[86] makes use of the fact that there is great regularity in the development of the centers of ossification in the fetus, and that in their consecutive appearance and large number they afford a check, as it were, one on another. The presence or absence of these is easily determined by the roentgenogram. The actual time of the anatomic appearance of the various centers is about one week ahead of the time at which they cast shadows in the roentgenogram large enough to be visible.

Basing his fact on the ronetgenographic study of a series of 55 normal fetuses whose ages had been determined from the history of menstruation and of pregnancy and from their measurements, and comparing his results with the roentgenographic studies of Bade, Hasselwander, and Lamberts, Hess concludes that the roentgenographic method of determining the age of the fetus is more reliable than determination of age based on length and other measurements, since osseous development is more regular and offers many more factors for consideration; one part of the body is a criterion of normality for the other parts, and pathology may often be readily recognized. Excellent reproductions of roentgenograms accompanied by diagrams of the fetuses of various ages, from 7 weeks onward, are included in the paper.

Heat Equilibrium.—In an article in 1915, McClure and Sauer[87] stated that studies of the relation of heat to the high infant mortality of summer have not yielded uniform results, and attributed this to neglect of an important internal factor. The external factors such as food, high outdoor and indoor temperatures, circulation of air, etc., had received most of the attention; while the most important internal factor, that is, the heat regulatory power of the infant, had been neglected.

Heat equilibrium of the organism depends on the proper balance between heat production and heat elimination. Heat production is influenced chiefly by food (Rubner) and work (well shown by Howland). Heat elimination is dependent almost entirely on (1) radiation; (2) conduction, and (3) evaporation.

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[86] Hess, Julius H.: Diagnosis of Age of Fetus by Roentgenograms. Am. Jour. Dis. Child., 1917, **14,** 397.

[87] McClure and Sauer: Clothing as a Factor in the Production of Heat Stasis. Am. Jour. Dis. Child., 1915, **9,** 490.

Loss by radiation and conduction is proportional to the difference between the surface temperature of the body and that of the surrounding air; it becomes zero when the difference is nil; good circulation of air aids this heat loss. Evaporation gains in importance as a means of heat loss at high temperature, coincident with the appearance of visible perspiration, and becomes the principle means of heat loss when the temperature of the surrounding air is higher than that of the body. Rubner showed the importance of heat loss by evaporation from the skin and lungs at high temperatures, and Mendelssohn found the mechanism of the heat regulation for the infant to be more efficient at high than low temperature. Studies by Helmholz[88] led him to believe that the direct effect of heat alone must be considered of relatively little importance. When heat, humidity, and diet were quite uniform, certain infants thrived, others sickened, pointing thus to some other factor allowing of greater individual variability. Such a factor he thought he found in clothing.

McClure and Sauer[87] then studied the effect of clothing on the loss of body heat in 4- to 6-weeks-old puppies. The jacketed puppies regularly showed a higher temperature than controls, the stools were frequently disturbed, and the puppies died shortly. The probable importance of overclothing as a factor in infant mortality was thus emphasized.

In a succeeding study McClure and Sauer[89] sought to furnish some more accurate data showing the influence of clothing on the heat regulatory power of the infant, particularly at high temperatures. By means of mercury thermometers and thermo-elements they determined the surface temperature of infants under different conditions of clothing and room temperature and humidity. The infants wore ordinary hospital clothing consisting usually of a thin cotton gown, double-breasted cotton undershirt, cotton hose and diaper. They were tested both clothed and five minutes after being unclothed. That clothing inhibits heat loss is well known. This is further emphasized by the fact that the temperature of the skin beneath the clothing is found to be higher than that of the same area when unclothed. McClure and Sauer tabulate their determinations, and then point out certain existing inexactnesses. Accepting their figures, however, with all due reservation, as the basis of calculation for the heat loss by

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88. Helmholz: The Relation of Heat to the Morbidity and Mortality of Infants from Gastro-Intestinal Diseases. Jour. Am. Med. Assn., 1914, **63,** 1511.

89. McClure, W. B., and Sauer, L. W.: The Influence of Clothing on the Surface Temperature of Infants. Am. Jour. Dis. Child., 1915, **10,** 425.

conduction and radiation, they hold it is evident that the *clothed* infant at a moderate room temperature is capable of availing itself of only about 68 per cent. of the possible heat loss due to these factors. At high room temperature it can only avail itself of about 24 per cent. of this possible heat loss.

At a room temperature of about 88 F. (31 C.) an infant clothed in the manner described and under the conditions of their experiment, from 24 to 30 per cent. humidity, etc., approaches very closely the point where a heat loss by conduction and radiation from the body surfaces is no longer possible. The preceding study on puppies shows this state of affairs may be fraught with danger to the organism.

A third and most recent paper by the same authors[90] takes up the question of loss of body heat through evaporation, the last mentioned of the three factors, radiation, conduction, and evaporation.

Heat loss by evaporation may occur (1) from the lungs, (2) from visible perspiration, and (3) from the so-called insensible perspiration. It is data in regard to the evaporation of water from the surface of the body as insensible perspiration that McClure and Sauer now report.

Observations by Loewy[91] made on individuals whose skin was devoid of sweat glands, would seem to demonstrate that insensible perspiration is entirely independent of the sweat glands. In infancy insensible perspiration would seem to be of special importance because the sweat glands "usually do not functionate during this period of life." The determination of the insensible perspiration from the total skin surface would be desirable, but such a procedure, if at all feasible, would be very difficult indeed. McClure and Sauer present some data with regard to the loss of water from restricted areas of the skin, as determined by a method which they consider superior to that used by Galeotti and Macri.[92]

As the result of these studies they conclude that, in so far as determinations of the loss of water vapor from a restricted skin area permit of conclusions with regard to the loss of water vapor from the skin in toto, it appears that the loss of water vapor from the skin is sufficiently great to make it an important factor in the heat elimination of the infant; that the rate of ventilation has a decided effect on the amount of water vapor given off by the skin, the amount increasing with the rate of ventilation up to a certain point, when it seems that a cooling effect prevents further increase; and finally, that cotton garments (two layers of cotton material as in ordinary hospital clothing) do not seem to offer any obstacle to the loss of water vapor from the skin, at least not when they have been in contact with the skin for a number of hours.

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[90] McClure, W. B., and Sauer, L. W.: Observations Regarding the Loss of Water Vapor Through the Skin in Infants. Arch. Int. Med., 1918, **21,** 428.

[91] Loewy: Biochem. Ztschr., 1914, **67,** 243.

[92] Galeotti and Macri: Biochem. Ztschr., 1914, **67,** 472.

Blood of Mother and Fetus.—Arthur Morse, in a study of the amino-acid nitrogen in the blood in normal and complicated pregnancies and in the new-born infant,[93] says that since the work of Fischer and Kossel teaches that the protein molecule is composed of amino-acids, we assume a close analogy exists between the synthesis of polypeptids in the laboratory and the synthesis of protein in the body. Moreover, it is natural to believe that fetal protein is built of amino-acids supplied from the mother's blood. From this standpoint peculiar interest attaches to the blood of pregnant women. One would like to know whether the maternal blood contains an unusual quantity of amino-acids during pregnancy, how the quantity of these substances in the blood of the mother compares with that in the blood of the fetus, and whether in the presence of auto-intoxications abnormal values are encountered in either circulation. With the Van Slyke method these problems may be profitably studied, though recognizing that the findings are not complete.

As the result of the study Morse concludes that the requirements of the fetus cause no increase of amino-acid nitrogen in the blood of pregnant women, over that found in normal women—8 to 14 mg. per 100 c.c. of blood; that, generally, normal values are found in pre-eclamptic toxemia and eclampsia, though exceptionally an increase appeared during convalescence; that nephritic toxemia is accompanied by normal quantities; while an excessive quantity of amino-acids occurred in cases of obscure toxemia, possibly related to acute yellow atrophy of the liver. During labor normal values were found; at its conclusion the extremes encountered were 8.1 and 13.9 mg.

In the fetal blood the amino-acid nitrogen varied between 10 and 15.8 mg. per 100 c.c. of blood. "The passage of amino-acids from mother to fetus requires the assumption of 'absorption' properties on the part of the placenta; for though the difference between the concentration of amino-acids in the two circulations is small, it is in favor of the fetus in 70 per cent. of the cases; and the higher level in that organism prevents the acceptance of simple diffusion as the explanation for the placental exchange. The 'absorption' property of the placenta probably protects the fetus against loss of material intended for construction of protein."

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[93] Morse, Arthur: The Amino-Acid Nitrogen of the Blood in Cases of Normal and Complicated Pregnancy, and Also in the New-Born Infant. Bull. Johns Hopkins Hosp., 1917, **28,** 199.

Courtney and Fales,[94] in the course of some studies on nutritional infants, made a large number of determinations of the total solids of the blood, and the chlorid content of the plasma, about eighty determination of each, on sixty-seven different children, ranging from 5 weeks to 6 years of age, though most of them were under 2 years of age. These they report.

Gettler and Baker[95] carried out a very complete investigation of the blood of normal adults. Courtney and Fales find that the values for the chlorids in normal infants are almost identical with those for adults. The figures for total blood solids are lower in infants, 16 to 18, as against 20 to 25 per cent. of the total blood in adults. Lust's (1911) findings for infants correspond.

In general, all infants not in a normal condition had low blood chlorid, but, except in edema or under some unusual condition of blood concentration, the percentage of total solids in the blood of infants tended to remain constant. Children suffering from tetany showed a tendency to slightly higher total solids and higher chlorid in the plasma than was found in any of the other pathologic conditions studied. Children suffering from malnutrition and digestive disorders showed the lowest chlorid in the plasma of all those investigated. Those with nutritional edema all showed abnormally dilute blood. Infants with sclerema had nearly normal total solids in the blood, with chlorid in the plasma like that of other pathologic cases, excepting the marasmus group. There was no constant relation between the variations in total solids of the blood and those in chlorid of the plasma. Saline-hypodermoclysis seemed to affect the percentage of total solids very little, but to raise the chlorid in the plasma nearly to normal.

Teeth.—Wall[96] says that while the lesions produced by the virus of hereditary lues in the second incisors—Hutchinson's teeth—are well known, little attention is paid by clinicians to the lesions in the other permanent teeth. Dental literature contains more references to this subject; especially to be recommended is the exposition of the subject by Cavallero.[97] As Cavallero remarks, "The dental stigmata are far from being restricted to Hutchinson's teeth. We must look for them in the whole dental system, in different forms, in arrangements, alterations, and even in the absence of some of the dental units." Fournier enumerates the dental stigmata pathognomonic of hereditary syphilis as follows: (1) Hutchinson's teeth; (2) cuspal erosions of the first permanent molar; (3) multiple and systematic dystrophies of the permanent teeth.

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[94] Courtney, A. M., and Fales, H. L.: Variation in Infants of Total Blood Solids and the Concentration of Sodium Chlorid in the Plasma. Am. Jour. Dis. Child., 1917, **14,** 202.

[95] Gettler and Baker: Jour. Biol. Chem., 1916, **28,** 211.

[96] Wall, Joseph S.: The Significance of Certain Dental Stigmata of Congenital Syphilis. Arch. Pediat., 1917, **34,** 765.

[97] Cavallero: Dental Cosmos, 1908, **1,** 167.

The temporary teeth calcify during the early months of pregnancy —dentification of the first or temporary set takes place during the first three or four months of pregnancy—and they remain unaffected, or death of the fetus takes place from abortion.

The sixth year molar is the *only* member of the permanent set to dentinify during intra-uterine life; the process usually begins about the fifth or sixth month. Passini, in 1907, demonstrated *Spirochaetae pallida* in the dental sacs of a 7-month-old fetus, findings which were later confirmed by Cavallero. All the other permanent teeth calcify after birth. The incisors and canines calcify in the first few months after delivery. Which teeth are affected may depend on the time at which the infection is most active. The changes in the incisors are generally known.

The changes in the sixth year molar, which may be the only dental deformity noted, in some instances are sufficiently characteristic to be of diagnostic use. There is erosion, disintegration, of the grinding surface. "The erosion is irregular in form, the surface of the molar for a third or a half or even the whole of its surface, is pitted, excavated, and discolored. There is often a pulpy looking mass of a dirty yellow color occupying most of the face of the crown, margined as it were by the line of cusps ordinarily found on the molar teeth. The tooth has been called 'the honey-comb molar of hereditary syphilis'—it is also referred to as a 'mulberry tooth,' from its resemblance to the tip of a mulberry."

Wall thinks the occurrence of such a molar is a point of great diagnostic importance and that it is not sufficiently recognized, especially as a clue to the presence of congential syphilis before the onset of a destructive keratitis. Photographs of casts of teeth accompany the article.

Tumors and Malformed Viscera.—An instance of primary sarcoma of the lung in a boy of 5 years is reported by Parkinson.[98] The child had been discharged from a surgical ward after an operation for inguinal hernia some ten weeks before his death. Shortly afterward a cough and difficulty of breathing had appeared. The symptoms progressed until the time of his death and wasting became marked. The heart was much displaced, a small immovable nodule appeared on the second rib, and bloody pleuritic effusion developed.

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[98] Parkinson, J. Porter: Primary Sarcoma of the Lung. Brit. Jour. Child. Dis., 1918, **15,** 28.

At necropsy the left lung was found to be replaced by a soft, friable, hemorrhagic growth, firmly adherent to the adjacent structure. The bronchial glands were involved in the mass of the growth. Microscopically the appearance was that of a small round-celled sarcoma.

Holmes[99] reports a case of ectopia cordis in a 15-month-old infant with necropsy findings. Three forms of ectopia cordis are recognized: (1) the *cervical heart,* in which the organ is displaced high in the neck; (2) the *pectoral heart,* with fissure of the sternum; and (3) the *abdominal heart,* in which the organ has passed through a defect in the diaphragm and into the abdominal cavity. Such anomalies are not extremely rare; they are found most frequently in prematurely born fetuses.

The anatomist Haller (1706) described a case; Peacock, in 1886, cited thirteen cases and described a fourteenth. Ballantyne, in 1904, mentioned nine additional cases, and another was described by Goode in the same year. Other American cases are those reported by Holt, Jacobi, Ellis and Welch.

The description of the present case is accompanied by illustrative plates. A photograph of the patient shows a tumor mass in the epigastrium, emerging from under the costal angle and extending downward almost as far as the umbilicus. This mass at birth was "raw" and bright red; later it became covered with skin. The roentgenogram shows enlargement of the heart to the right and lines suggestive of a defect in the diaphragm. The tumor mass was firm and pulsated. It was thought during life to be a misplaced heart. At necropsy it was found to be a misplaced left ventricle. Drawings show the relation of this to the rest of the heart.

The displaced portion of the heart (left ventricle) lay below a rounded muscular mass representing a hypertrophied right ventricle, and to the left of it. From it proceeded an elongated aorta. Into it opened a small mitral valve (0.6 cm.). Communication with the right ventricle occurred through a large circular defect (1.5 cm.) in the interventricular septum. In the main the circulation of the blood followed the usual channels. The small size of the left ventricle was compensated for by the assistance given by the hypertrophied right ventricle. The whole was inclosed in an irregular pericardial sac, and lay above the diaphragm, which found attachment anteriorly at an abnormally low level.

Two cases of congenital heart defects are reported by Bergmark.[100]

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[99] Holmes, James B.: Ectopia Cordis, with Report of a Case in a 15-Month-Old Infant. Johns Hopkins Hospital Rep., 1917, **18,** 287.

[100] Bergmark: Svensk. Läk. Sällsk. handl., 1917, **43,** 553.

Comby[101] has reported an instance of obliteration of the inferior vena cava in a boy of 12 years.

Pyloric Stenosis.—Pylorospasm and congenital pyloric stenosis have been the subject of numerous papers during the past months. The case described by the American physician, Hezekiah Beardsley, in 1788, entitled a Case of Scirrhus in the Pylorus of an Infant, and identified in 1903 by Osler as "congenital hypertrophic stenosis of the pylorus," has been regarded as the earliest published case. The symptoms in this case appeared shortly after birth, and persisted up to the time of the child's death at 5 years of age. Foote[102] now calls attention to earlier work by an English pediatrist, George Armstrong, saying:

> While Beardsley's monograph still stands as the first separate publication dealing with pyloric spasm and stenosis, the distinction of describing and actually naming with the term we now use the symptoms and pathology of this disease of the new-born apparently belong to George Armstrong, an English pediatrist, whose work appeared in 1777, a textbook entitled "An Account of the Diseases Most Incident to Children from Their Birth to the Age of Puberty, with a Successful Method of Treating Them," etc. (London, 1777). This textbook was accorded several reprintings, and was rewritten by Buchan in 1808. Clinical postmortem findings, a typical case history, and a family history, including three similar cases, led Armstrong to conclude that a child which he had treated for "watery gripes," died from spasm of the pylorus.

The postmortem findings in the case of an infant that died about three weeks of age are described, with the statement that "it looked as if the disease had been chiefly owing to a spasm *in the pylorus*, which prevented the contents of the stomach from passing into the duodenum."

In a paper entitled "Hypertrophic Stenosis in Infants" Holt[103] presents data derived from the study of 141 cases. The clinical course and the uniform pathologic findings have convinced his colleagues as well as himself that a division of cases of pyloric stenosis of infants into spasmodic and hypertrophic types is not admissible. It is his firm belief, based on observation of these cases in the early weeks, that in all of them hypertrophy precedes the tonic spasm; but that the hypertrophy continues long after the spasm has subsided he has absolute proof.

The clinical picture presented by a case is a striking one and in the large majority of the cases seen it is remarkably uniform. If one is familiar with the condition the diagnosis of hypertrophic stenosis is in most instances easy, for the symptoms in fully four-fifths of the cases are classical. Enumerated in the order of their diagnostic importance Holt would place the diagnostic points in the following order: (1) the history, if obtained from a reliable mother or nurse; (2) abnormal gastric retention, observations being repeated four or five times at least; (3) peristaltic waves, not of diagnostic value unless typical; (4) the presence of a palpable tumor; (5) wasting, constipation, scanty urine, etc. The roentgen ray adds nothing of importance which cannot be discovered by a study of gastric retention and without its dangers.

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[101] Comby: Arch. de méd. d. enf., 1917, **20,** 418.

[102] Foote, J.: Pylorospasm and Congenital Pyloric Stenosis. Am. Jour. Dis. Child., 1918, **15,** 351.

[103] Holt, L. E.: Hypertrophic Stenosis in Infants. Brit. Jour. Child. Dis., 1917, **14,** 161.

Many of the milder cases recover with only medical treatment. This is described. All infants which do not improve under such treatment in the course of two or three weeks, and the more severe types in a much shorter time, should be treated surgically. Cases which come under observation after four or five weeks of vomiting and marked loss in weight are best treated by operation as soon as the diagnosis is established. Earlier operations should be abandoned for the simple external division of the circular muscular fibers proposed by Rammstedt.

Examination of the tumor in longitudinal section—it is usually about as large as a peanut or the last phalanx of the little finger, of glistening whiteness and cartilaginous hardness—shows that the hypertrophy is practically limited to the circular muscular layer. The circular fibers are much increased both in size and number; there is a true hypertrophy. In recent cases there is usually a considerable amount of edema. The longitudinal layer of muscular fibers, the submucous and mucous coats, are in most cases quite normal. Rammstedt, of Munster (1913), simply divided the circular muscular layer of the pylorus by external incision. The stomach is unopened; the operation in skilled hands is short; the patients make excellent recoveries.

Patients followed two and three years after the Rammstedt operation show no interference with health and progress; patients not operated on usually show no symptoms after the first year; yet the possibility exists that this condition may be the basis of pyloric obstruction in later life.

Ladd[104] contributes a paper on the same subject.

Ransohoff and Wooley[105] and later Rachford[106] describe the conditions found postmortem at the pylorus in a 7-month infant that died suddenly four months after a Rammstedt operation had been done. The clinical history had been typical. At operation the pyloric tumor was of cartilaginous hardness, 2 cm. long and 1 cm. thick. The child's recovery after the operation had been rapid and uneventful, and at the age of 6 months it appeared in every way normal. In the middle of the seventh month the child without warning was found dead in bed. Death was attributed to the unusually large thymus (65.5 gm.).

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[104] Ladd, W. E.: Congenital Pyloric Stenosis. Boston Med. and Surg. Jour, 1918, **178,** 767.

[105] Ransohoff, J. Louis, and Wooley, Paul G.: Operative Cure of Congenital Pyloric Stenosis; Thymic Death after Seven Months: Necropsy. Jour. Am. Med. Assn., 1917, **68,** 1543.

[106] Rachford, B. K.: Pyloric Stenosis in Infancy. Arch. Pediat., 1917, **34,** 803.

At necropsy it was found that along the anterior surface of the pylorus there was a shallow linear depression approximately 2 cm. long, which represented the scarred site of a previous surgical incision, and in the groove and its margins were tags of old fibrous adhesions, rather tenuous in texture, which had united the pylorus to the adjacent tissues. The tumor mass had disappeared. Section showed that from the bottom of the groove to the submucosa was a band of fibrous tissue which represented a loss of muscular tissue in that region. There was no bulging, no diverticula or hernia formation. It seemed possible that the muscular layers were somewhat better developed than would be called normal, but the variation seemed too slight for weight to be attached to it. The appearance of the pylorus on section was as if a ring shaped muscle were supplied at one point with a tendon.

It appeared that the surgical incision permitted the muscular coats of the tissue to retract and the opening to gap, and that subsequently the space was filled with organized tissue, which in its fully developed state was fibrous tissue. It seemed also that during the healing of the wound the pyloric orifice became dilated and then remained so, and thereafter performed its function in an acceptable manner. There is thus afforded anatomic proof of the perfect efficiency of the Rammstedt operation.

Scott[107] reports a case of hypertrophic pyloric stenosis in a 2-year-old child with operation (Rammstedt) and death. In Scott's case there was no early history of vomiting—though he had occasionally done so during "teething," and after eating a banana. He had passed through whoopingcough. About a month before the operation he had become nauseated and had vomited following a hypodermic injection given to produce vomiting, and occasionally thereafter. There was an indefinite history of chewing firecrackers. The child presented a scaphoid abdomen with visible peristaltic waves but no palpable tumor. Six days after entrance to the hospital, it was thought advisable, as the child was getting weaker, to operate.

Operation revealed "a typical hypertrophied pylorus such as is seen in congenital pyloric stenosis." An incision (Rammstedt) showed typical cartilaginous texture. The mucosa was accidentally nicked. The child died, with rising temperature (104.6 F.). Necropsy was not permitted.

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[107] Scott, A. J., Jr.: Hypertrophic Pyloric Stenosis in a Two-Year-Old Child; Report of a Case. Jour. Am. Med. Assn., 1918, **70**, 1918.

The first reported case of pyloric stenosis in an older child is that by Beardsley (referred to in the foregoing) in which a boy showed symptoms shortly after birth, and up to his death at the age of *5 years*. In 1914, Shaw and Elting reported a case in which the patient showed symptoms from the seventh or eighth month, but was not operated on until the age of 16 months. The child lived.

Arreger reported a case in which the patient had no symptoms until he was 3 years old, and at the age of 5 years had the first marked symptoms. He was not operated on, however, until he was 6½ years old.

Grey,[108] after performing a gastric fistula on dogs as devised by Janeway, found it possible to dissect a 2 cm. long cylinder of duodenum containing the major bile duct and insert it into the posterior wall of the stomach, anastomose the ends of duodenum, and tie off the lesser pancreatic duct. The operation was readily carried out through a high right rectus or midline incision.

From the results of his experiments it appears that the presence of a considerable amount of pancreatic juice in the stomach throughout the period of digestion leads only to a moderate decrease in the acidity level of the ingesta in the late stage of digestion. Earlier in the process there is no constant alteration in the acidity level in either direction. The findings then serve not only to corroborate the views of Boldyreff, but also to demonstrate the remarkable compensatory activity of the gastric glands, under conditions which entail an unusual quantity of alkali in the stomach.

In addition the work has shown that when the larger pancreatic duct is properly transplanted into the wall of the stomach, it may remain patent for months. In animals in which the operation has been carried out, the pancreas has been found to undergo no inflammatory or other changes. The finding is regarded as evidence against the postulation of Illava that gastric juice is probably responsible for the occurrence of certain cases of acute hemorrhagic pancreatitis.

Carcinoma.—Cosens[109] has reported an instance of primary carcinoma of the stomach in a boy.

Primary carcinoma of the liver in early life, though very rare, has been the subject of considerable study. Reported cases have been tabulated by Steffen and Philipp and Castle (1914). Griffith[110] analyzes the tabulations and adds twelve others from the medical literature and one of his own. This brings the total reported cases regarded by Griffith as authentic up to fifty-seven.

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[108] Grey, Ernest S.: The Diversion of the Pancreatic Juice from the Duodenum Into the Stomach. Its Effect on the Level of Gastric Acidity and on the Pancreas. Jour. Exper. Med., 1917, **26,** 285.

[109] Cosens: Brit. Med. Jour., 1917, **1,** 649.

Of these 57 cases, 25 were in males and 26 in females. In the other instances the sex is not stated. The age of the patients varied from birth to 16 years. In two instances the age is not stated. Four were new-born, and including these there were 8 in the first three months, and 16 in all in the first year. The remainder were divided as follows: 1 to 2 years, 8; 3 years, 2; 4 years, 2; 5 years, 2; 6 years, 2; 7 years, 2; 8 years, 1; 9 years, 3; 11 years, 4; 12 years, 5; 13 years, 7; 14 years, 3; 15 years, 2; 16 years, 1.

The occurrence of so many early cases suggests the existence of a tumor of an embryonal nature; and this has been claimed for a number of them. Others are simple carcinoma; others clearly adenocarcinoma; and others, doubtless some of them carcinomatous, have been described as adenoma. The tumors may appear in various forms and may be divided (Eggel) into nodular, massive, and diffuse, the first being most common, the last rare. Metastases are not uncommon, especially to the lungs and to other parts of the liver. Operative interference has been attempted in one instance but without success. It would seem possible only in cases of a single encapsulated tumor. In view of the seriousness of the condition, any effort at removal would seem justifiable.

Griffith's case was a female infant, aged 21 months. She had previously been in good health except for some degree of anemia, which was supposed to be dependent on indigestion, and a constant tendency to constipation. The tumor had been discovered accidentally five weeks before. It was said not to have increased in size, but there was an unusual amount of veining of the walls of the thorax and of the distended abdomen; the child had lost weight and had not seemed well. Examination showed a smooth hard mass just below the costal border and midway between the midsternal and right mammary lines. It changed its position distinctly with respiration. A roentgen-ray picture seemed to show opaque bodies in the tumor mass, thus suggesting a diagnosis of teratoma connected with the kidney or with the suprarenal body. Exploratory incision revealed an orange-sized mass in the right lobe of the liver. It was covered by a dark gray, glistening, fibrous capsule, projected slightly above the surface of the liver, and extending in depth through the entire thickness of the lobe. There was no evidence of infiltration of the hepatic tissue beyond the

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110. Griffith, J. P. C.: Primary Carcinoma of the Liver in Infancy and Childhood, Am. Jour. Med. Sc., 1918, **155,** 79.

capsule, nor of metastasis. Incision into the capsule showed a soft, whitish substance, much resembling in color and appearance the thymus gland or pancreas.

Histologic examination showed the tissue to consist entirely of epithelial cells without trace of liver tissue. Histologically it was a carcinoma simplex, but the presence of attempts at tube arrangement suggested that the growth was originally a cancer of the bile ducts.

Forman and Hattery[111] report a case of primary carcinoma of the liver in a boy of 3 years. Attacks of abdominal distention and pain had appeared a year earlier and grown progressively more severe. They were accompanied at times by jaundice. There was great enlargement of the liver and loss of weight. The tumor fell into the class of primary parenchymatous carcinomas of the liver, usually regarded as congenital. The specimen served to emphasize the usual absence of extra hepatic metastases in cancer of the liver.

An instance of primary carcinoma of the liver in a girl of 11 years is reported by De Saussine.[112]

Ganguli[113] writes upon Infantile Biliary Cirrhosis.

Miscellaneous Pathologic Visceral Condition.—Cockayne[114] reports a case of congenital defect of the duodenum in which bile was found both above and below the absent portion. The child was a male infant born at full term, which died on the fifth day with symptoms of intestinal obstruction. The vomitus was invariably watery and green. At the confinement the medical attendant had noticed that the liquor amnii was excessive in quantity and bright green in color. At necropsy the first part of the duodenum was found to end blindly, to be greatly distended and globular in outline, and to contain *bile-stained* fluid. The pancreatic duct entered the posterior aspect of the blind sac. There was no connection except by peritoneum with the upper blind sac and the narrow commencement of the lower part of the duodenum, not even a thin cord. The bile duct opened directly into the narrow commencement of the lower part of the duodenum. The gallbladder, liver, and ducts were normal and contained bile. Careful search failed to reveal any second bile duct, leading to the upper portion of the duodenum.

The source of the large quantity of bile-stained fluid that was vomited is the interesting feature of the case. The earliest case in which bile was found both above and below a duodenal occlusion was described by Hirschprung, who proved the presence of bile pigments in the stomach. Later cases have been reported by Wilks, Hobson, Wyss, Cordes and others. Cordes proved conclusively that in her case the common bile duct sent a small branch to the dilated duodenum above the occlusion, and gave reasons for believing that the anomaly might be present in other cases. The view of Wilks that the green fluid vomited is a secretion of the stomach may be rejected. The only reasonable alternative to Cordes' explanation is that the child may have swallowed bile-containing amniotic fluid; this seems unlikely, and in one case (Anderson's) it was specially noted that the amniotic fluid was colorless.

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[111] Forman, F., and Hattery, J. S.: Primary Carcinoma of the Liver in Childhood; Report of a Case. Am. Jour. Obst., 1917, **76**, 862.

[112] De Saussine: Arch. de méd. d. enf., 1917, **20**, 472.

[113] Ganguli: Indian Med. Gaz., 1917, **52**, 361.

[114] Cockayne, E. A.: A Case of Congenital Defect of the Duodenum in which Bile Was Found Both Above and Below the Absent Portion. Brit. Jour. Child. Dis., 1917, **15**, 188.

An instance of common cyst of the bile duct is reported by E. Waller.[115]

Eisendrath[116] reports two cases of gallstones in girls of 15 years; in the second case there was an accompanying acute cholecystitis with many calculi. Up to 1913, Khantz was only able to find the reports of fifteen cases; of these, one was in a new-born infant, five were necropsy observations, and in nine the diagnosis was confirmed, as in Eisendrath's cases, by operation. One other case has since been reported. All of the patients above 13 were girls. The stones may be numerous.

C. Martelli[117] reports a case of heart disease in a child under 3 years with ascites from the liver.

Scott[118] reports an instance of pneumococcal abscess of the liver in a 13-month-old infant, suffering from pneumonia. At necropsy there was seen a prominent bulging on the upper surface of the liver, and on opening this there was a marked outpouring of greenish pus, which on smear and culture showed pure culture of pneumococcus.

Jemma[119] reports a case of abscess of the liver in a boy of 8 years.

The subject of congenital variations in the peritoneal relations of the ascending colon, appendix, cecum, and terminal ileum has been studied by S. C. Harvey.[120]

Vander Bogert[121] reports a fourth case of congenital atresia of the small intestine. The child died four days after birth. The symptoms were those of complete obstruction. The vomitus became distinctly

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115. Waller, E.: Hygiea, Stockholm, 1917, **79,** 513.

116. Eisendrath, D. N.: Gallstones in Infancy and Childhood. Ann. Surg., 1917, **66,** 557.

117. Martelli, C.: Pediatria, Naples, 1917, **25,** 401.

118. Scott: California State Med. Jour., 1918, **16,** 337.

119. Jemma: Pediatria, Naples, 1917, **25,** 129.

120. Harvey, S. C.: Congenital Variations in the Peritoneal Relations of the Ascending Colon, Cecum, Appendix and Terminal Ileum. Ann. Surg., 1918, **67,** 641.

121. Vander Bogert, Frank: Congenital Atresia of the Small Intestine, Arch. Pediat., 1918, **35,** 45.

fecal on the third day. Enemas yielded a mucus cast partially filled with a substance resembling meconium, except that it gave no reaction for bile. (Normal meconium gives a bile reaction.) Necropsy showed the obstruction to be complete, the small bowel much dilated, ending abruptly 25 inches above the ileocecal valve. There was complete absence of intestine for about ½ inch and both the small and large bowel below were poorly developed.

In the three cases earlier reported (*Arch. Pediat.*, 1916, 33, 194) the stools obtained by enema were normal in character, and the obstruction was incomplete. In the present case, as in the earlier complete case, bile appears to have been absent. Vander Bogert feels this should be regarded as conclusive proof of complete obstruction.

St. George[122] reports a case of congenital obstruction of the intestines. The patient, a girl, the second of twins, died on the seventh day after birth. A clinical diagnosis of intestinal obstruction (congenital) and hemorrhagic disease of the new-born was made. At necropsy there was found an apparently complete stricture of the duodenum about 9 cm. below the pylorus, and another in the jejunum about 20 cm. below. Microscopic section showed "complete destruction of the lumen of the duodenum and replacement by fibrous tissue in which were a number of blood vessels." Section through the second point of constriction showed a lumen which was markedly diminished in caliber and occupied by a small blood clot.

In the large necropsy service of Bellevue Hospital during the past fourteen years congenital obstruction of the intestine has been encountered twice only. References to 143 cases in the literature are appended.

Griffith[123] reports a case of idiopathic dilation of the colon, in a colored boy of 4 years. The condition had been present from his early days. His general health had always been good and while the case appeared to be a typical one of moderate degree, operative interference did not seem justifiable.

The case is reported because of the interesting roentgenogram that was obtained. Griffith distinguishes between secondary dilatation of the colon due to abnormal construction, stenosis, and the like, and Hirschprung's disease, which is in no way associated with stenosis and appears to be due to a congenital tendency for the colon to dilate. This tendency is present at birth although the actual dilatation may not show itself for some time.

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[122] St. George, A. V.: Congenital Intestinal Obstruction; with the Report of a Case. Am. Jour. Dis. Child., 1918, **15**, 354.

[123] Griffith, J. P. C.: A Case of Idiopathic Dilatation of the Colon, with Photograph and X-ray. Arch. Pediat., 1918, **35**, 36.

Another case with roentgenograms is reported by Baird and Kindley.[124] Their patient was a 6-year-old girl. Symptoms had appeared at 3 years. She was pale but not emaciated. The abdomen was distended. A firm mass extended from the right hypochondrium down to the pelvis and then upward to the left hypochondrium. Bismuth given at night appeared next morning in a channel extending at least partly through the mass, apparently involving the first part of the transverse colon. On moving the mass the barium could be seen to move.

Schneiderhohn (1915) found 358 cases of this condition in the literature and added four of his own. A number of others have been added. Other cases are reported by Finchietto,[125] Noble[126] and Sohmer.[127] Neugebauer (1913) advised resection and gives 56.5 per cent. of cures after immediate resection and 90 per cent. when it is done in stages. Schneiderhohn showed that of 151 cases treated medically, 25 per cent. were cured, 81 per cent. of the cured being children.

Genito-Urinary Conditions.—Many studies on the elimination of pherolsulphonephthalein in children have been made since the substance was introduced into clinical medicine in 1910. It is an ideal substance for the study of renal function, being practically nontoxic and nonirritating, readily absorbed and readily eliminated through the kidneys. Rowntree and Geraghty believe "that the capacity for picking out the molecules of phthalein from the infinitely dilute solution in the blood and passing them on into the urinary secretion in comparatively concentrative solution, is a function specific to the kidney." They have also obtained fairly conclusive proof that the cells of the tubules play the most important rôle in the excretion of the phenolsulphonephthalein, the glomeruli eliminating a very much smaller amount.

In 1912 Smith reported the findings in a small series of young patients. Fishbein, in 1913, studied a small group of children and adults. In 1915 Tileston and Comfort estimated the phenolsulphonephthalein output in several groups of patients varying in age from 6 months to 11 years. Only six of the patients were under 2 years of age. In the same year Hempelmann studied the phenolsulphonephthalein elimination in seven patients with orthostatic albuminuria, from 8 to 12 years of age; and in the next year (1916) Barker and Smith reported the findings in similar patients from 16 to 25 years of age.

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[124] Baird, R. W., and Kindley, G. C.: Hirschsprung's Disease; Report of a Case. Southern Med. Jour., 1917, **10,** 846.

[125] Finchietto, R.: Megacolon. Rev. assoc. med. argentino, 1917, **27,** 873.

[126] Noble, T. B.: A Case of Megacolon. Am. Jour. Obst. and Dis. Women and Child., 1917, **76,** 946.

[127] Sohmer, A. E.: Congenital Idiopathic Dilatation of the Colon. Minnesota Med., 1918, **1,** 119.

Gittings and Mitchell's[128] studies in phenolsulphonephthalein elimination were made on seventy-five hospital patients varying in age from 3 weeks to 10 years; forty-four were under 1 year of age; seven from 1 to 2 years of age, and twenty-four from 2 to 10 years of age.

Their studies show that the age of the patient within this limit has no influence on the elimination; "even the youngest children and infants show about the same capacity for phenolsulphonephthalein elimination as do adults—60 per cent. for two hours and 45 for one hour, at 3 and 5 weeks." They confirm the observation that the elimination of phenolsulphonephthalein is not markedly decreased in any disease other than renal. They believe that in children a single collection exactly two hours after the injection into the lumbar muscles of 6 mg. of phenolsulphonephthalein, should be the method of choice. The necessity for continuous or repeated catheterization is thereby avoided.

The occurrence of multiple urinary calculi in a boy of 10 years is reported by Pybus.[129] Roentgen-ray examination revealed an oval calculus in the pelvic portion of the left ureter, and a second in the right kidney. The child had passed a stone per urethram three years previously. He had also been recently operated on with the extraction of a small stone which was impacted in the urethra. A few days later he passed a larger stone. The roentgenograms were then made. An accompanying cystitis was treated. A second plate made three months later showed the stones had not altered in position. They were then successfully extracted. The pyuria ceased and the child's condition, both physical and mental, underwent very great improvement. Cumston[130] shows how easily the presence of such stones may be overlooked. He then considers the technic of removing them.

Borobio,[131] Cifuentes[132] and Martin,[133] also contributed articles on renal calculi in childhood, the last mentioned reporting four cases.

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[128] Gittings, J. C., and Mitchell, A. G.: The Phenolsulphonephthalein Elimination in Infants and Young Children. Am. Jour. Dis. Child., 1917, **14,** 174.

[129] Pybus, F. C.: A Case of Multiple Urinary Calculi. Brit. Jour. Child. Dis., 1917, **14,** 97.

[130] Cumston, C. G.: A Note on Ureteral Calculi in Childhood. Brit. Jour. Child. Dis., 1917, **14,** 94.

[131] Borobio, P.: Bladder Concretions in a Child. Arch. espan. de pediat., 1918, **2,** 65.

[132] Cifuentes, P.: Calculi in a Child's Kidney. Arch. Espan. d. pediat., 1918, **2,** 26.

[133] Martin, A. P.: Hematuria with Kidney Stones—Four Cases. Siglo méd., 1917, **44,** 568; and Stones in the Ureters, Ibid., 1918, **55,** 124.

L. W. Hill[134] reviews the literature of the last nine years on nephritis of infancy and childhood.

Royster[135] reports the gross and microscopic findings in a case of bilateral polycystic kidneys in an 8-months-old male infant of Syrian parentage. The masses were evident at 4 weeks of age. The report is well illustrated.

An instance of congenital cystic kidney in which a tuberculous process was superimposed is reported by Woolley.[136]

Darnell[137] reports the occurrence of a mixed cell tumor of the kidney weighing 3 pounds, in a 10-months-old infant, and Kirmisson and Tretiakoff[138] report an adenosarcoma of the kidney in a girl of 6.

Mixter[139] reports an instance of sarcoma of the bladder in a young child.

Cuthbert[140] reports a metastatic glioma (neuro-epithelioma) of the right ovary in a child of 3 years.

The occurrence of typhoid gangrene in a girl of 5 years, requiring amputation, is reported by Vinache.[141]

Carcinoma of the breast in the male child is extremely rare. It has even been asserted that it does not occur. Blodgett, however, in 1897, reported a case in a boy of 12 years and Bryan reported a case in a boy of 14 years and 8 months. Simmons[142] now reports one in a boy of 13 years.

The patient was a well built, healthy boy. The family history was essentially negative. About a year earlier the boy had been struck in the right breast with a baseball bat. The blow was light and caused no immediate soreness, but soon afterward the boy noticed after exertion a burning and stinging sensation in that breast. About seven months later a swelling became noticeable and there was some tender-

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134. Hill, L. W.: Review of the Literature of the Last Nine Years on Nephritis of Infancy and Childhood. Boston Med. and Surg. Jour., 1917, **177,** 313.

135. Royster, L. T.: Polycystic Kidney in an Infant. Am. Jour. Dis. Child., 1918, **15,** 196.

136. Woolley, P. G.: A Case of Congenital Cystic Kidney in which a Tuberculous Process Was Superimposed. Jour. Lab. and Clin. Med., 1917, **3,** 55.

137. Darnell, W. E.: Mixed Cell Tumor of the Kidney Weighing Three Pounds in an Infant Ten Months Old. Am. Jour. Obst., 1917, **76,** 786.

138. Kirmisson, E., and Tretiakoff: Adenosarcoma of the Kidney in a Girl of Six. Arch. de méd. d. enf., 1917, **20,** 257.

139. Mixter, C. G.: Sarcoma of the Bladder in a Child. Ann. Surg., 1917, **65,** 628.

140. Cuthbert, Lockyer: Metastatic Glioma (Neuro-epithelioma) of the Right Ovary in a Child Aged 3 Years. Brit. Jour. Child. Dis., 1917, **14,** 199.

141. Vinache, A.: Un cas de gangiène typhoide chez un enfant. Paris méd., 1917, **24,** 402.

142. Simmons, R. R.: Adenocarcinoma of the Breast Occurring in a Boy of Thirteen. Jour. Am. Med. Assn., 1917, **68,** 1899.

ness. A diagnosis of chronic mastitis was made and the entire breast removed.

The diseased tissue was approximately 8 cm. across and about 1.5 cm. thick in the center; toward the margin the tumor was thin. The axillary glands showed no enlargement.

Microscopically there was a marked proliferation of the gland elements throughout the sections. The newly formed glands were very irregular in shape, and the epithelium was arranged in many layers. Some showed definite lumina, while in others the proliferation was so great that the lumen was entirely filled up with cancer cells. Many of the glandular structures showed an ingrowth of stroma dividing it up into many smaller divisions. There was a tendency toward the formation of grapelike clusters of these atypical glands. The ducts showed some reduplication in the layers of epithelium. The stroma was abundant but not highly cellular. The adipose tissue appeared normal except for some areas in which the cancer had grown into it. There was a tendency to degeneration of the cells which lay centrally in the atypical acini, but this had not progressed to a marked degree. The pathologic diagnosis was adenocarcinoma of the breast, of the medullary type. The case is unusual both from the standpoint of age and sex.

Ehrenfried[143] reports cases of hereditary deforming chondrodysplasia, and Opie and Allison[144] consider hypertrophic chondrodystrophy in infancy and adolescence, and Gibney[145] considers osteochondritis deformans juvenalis.

Pathology Related to the Nervous System.—Felton, Hussey and Bayne-Jones[146] in a preliminary report on the hydrogen-ion concentration of the spinal fluid, as determined by the colorimetric method, confirm the work of Besgaard, in which he states that the reaction of the cerebrospinal fluid is more acid than $pH = 8.1$. It is approximately that of the blood serum. Certain inaccuracies inherent in the colorimetric method of determination, as compared with the gas chain method, for determining the hydrogen-ion concentration of the spinal fluid are noted.

Reference was made last year to the studies of Schlapp and Gere[147] on eight cases of internal hydrocephalus of the obstructive type, with especial reference to obliterating lesions of the aqueduct of Sylvius as the cause of the ventricular distention. Schlapp and Gere thought it not unreasonable to attribute many if not the majority of cases of congenital internal hydrocephalus to closure of the aqueduct of Sylvius through proliferation of the glia and ependymal tissues, or to the invasion of the fourth ventricle by tumors.

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[143] Ehrenfried, A.: Hereditary Deforming Chondrodysplasia; Report of Cases. Am. Jour. Orth. Surg., 1917, **15,** 463.

[144] Opie, E. L., and Allison, N.: Hypertrophic Chondrodystrophy in Infancy and Adolescence. Progressive Anomaly of Osteogenesis. Jour. Med. Research, 1917, **36,** 277.

[145] Gibney, V. P.: Osteochondritis Deformans Juvenalis—Perthes Disease. Med. Rec., New York, 1917, **91,** 793.

[146] Felton, L. D., Hussey, R. G., and Bayne-Jones, S.: The Reaction of the Cerebrospinal Fluid. Arch. Int. Med., 1917, **19,** 1085.

[147] Schlapp, M. G., and Gere, B.: Occlusion of the Aqueduct of Sylvius in Relation to Internal Hydrocephalus. AM. JOUR. DIS. CHILD., 1917, **13,** 461.

Dandy and Blackfan,[148] following their earlier work, divide cases of internal hydrocephalus into two apparently distinct anatomic varieties—obstructive hydrocephalus and communicating hydrocephalus. In their second study[149] they conclude that "meningitis is by far the greatest etiologic factor in both types of hydrocephalus and probably always the cause of the communicating variety. This may be either prenatal or postnatal. The meningitis may be of a very mild grade and easily overlooked. Spontaneous recovery sometimes occurs. Their material comprised twenty-six cases, fifteen of the obstructive and eleven of the communicating variety. Postmortem examinations demonstrated an obstruction in every case in which an obstruction had been shown clinically by the phenolsulphonephthalein test. "Absorption of cerebrospinal fluid is a general process, from the entire subarachnoid space, and communicating hydrocephalus results because only a fraction of the area can be utilized for absorption." Still less is available in the obstructive type.

In a symposium on hydrocephalus Elsberg[150] expressed the opinion that cases of the congenital type are entirely different in genesis and course from those of inflammatory nature. There are, according to him, three definite types: that due to obstruction, that due to diminished absorption, and that due to hypersecretion. With hypersecretion the only thing to be done is to give relief by frequent puncture and administer thyroid preparations to diminish the amount of secretion.

Of forty cases of chronic hydrocephalus studied, ten were obstructive, thirty nonobstructive, and of these last eighteen were nonobstructive with diminished absorption and hypersecretion.

Elsberg found some evidence that puncture of the corpus callosum might be worth trying in patients with obstructive hydrocephalus in whom subarachnoid absorption had been demonstrated to be below normal. In cases of hydrocephalus due to hypersecretion, lumbar

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148. Dandy, W. E., and Blackfan, K. D.: Internal Hydrocephalus; an Experimental, Clinical and Pathological Study. Am. Jour. Dis. Child., 1914, **8,** 406; also Beitr. z. klin. Chir., 1914, **93,** 392.

149. Dandy, W. E., and Blackfan, K. D.: Internal Hydrocephalus. Am. Jour. Dis. Child., 1917, **14,** 424.

150. Elsberg, Charles A.: Chronic Internal Hydrocephalus. The Newer Methods for Its Recognition and Treatment. Abstr. Arch. Pediat., 1918, **24,** 851.

puncture should be done every few days (15 to 30 c.c. fluid withdrawn) and the patient should be given thyroid extract up to the physiologic limit. He felt convinced that real success could not be expected from any methods thus far devised to drain fluid into any cavities of the body (Mt. Sinai Hospital experience).

Dr. William Sharpe, on the other hand, felt that success had been attained by providing drainage through the dura into the subcutaneous areas of the scalp by means of linen thread (seventeen deaths in fifty-eight cases). From his observations at operation and at necropsy on fatal cases (fourteen out of forty-one) he believed most cases of hydrocephalus due to a form of meningitis and a blocking of the stomata of exit of the cerebrospinal fluid in the cortical veins and sinuses, and possibly lymphatics.

Dandy and Blackfan feel that the surgical treatment of internal hydrocephalus has now a definite anatomic basis and hopeful prospects.

Holt[151] reports a case of gliosarcoma in an infant of seven weeks that resembled hydrocephalus. At about 2 weeks of age the head was observed by the parents to be enlarging more rapidly than normal. A little later the veins of the scalp became very prominent. The picture of hydrocephalus was produced. The head increased greatly in size. It was somewhat asymmetrical, there being a very great prominence in the left frontal region. At 8 weeks a spontaneous rupture took place over this prominence, and a true hernia cerebri was formed. The child died two days later.

The tumor mass was found to involve practically the entire left hemisphere. It apparently grew from the floor of the lateral ventricle. Microscopic examination showed it to be a gliosarcoma.

Acute Infections.—Borries[152] reports constantly clear lumbar puncture fluid with severe "otogenous meningitis."

Davison and Miller[153] report clinical and bacteriologic observations on a case of meningitis due to a hitherto undescribed organism. The onset was sudden with convulsions, in a 6-months-old child which had been treated during the preceding three weeks for a purulent otitis media with moderate elevation of temperature. The physical examination was negative except for the double otitis media. The temperature was 102.6 F. The convulsions were promptly controlled with sedatives. Lumbar puncture yielded purulent fluid, without organisms.

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[151] Holt, L. E.: Gliosarcoma in an Infant of Seven Weeks. Resembling Hydrocephalus. Am. Jour. Dis. Child., 1917, **14,** 219.

[152] Borries, G. V. T.: Lumbar Puncture Fluid Constantly Sterile with Severe Otogenous Meningitis. Ugesk. f. Læger, 1917, **79,** 997.

[153] Davison, W. C., and A. S., and Miller, M. K.: Meningitis in an Infant Due to Hitherto Undescribed Organism, Micrococcus Florens. Jour. Exper. Med., 1917, **26,** 779.

Antimeningococcus serum was administered. Symptoms of meningitis appeared. The injections were continued. The fluid became almost clear but contained many cells.

On the twenty-ninth day of the disease there was an abrupt rise of temperature, and a reappearance of signs of acute meningitis. The eighteenth lumbar puncture yielded very cloudy fluid in which, for the first time, organisms were demonstrable in great abundance in both films and cultures. They were gram-negative intracellular and extracellular diplococci, many of them arranged in groups of twos and threes. They continued to be present in the greatest abundance, and, later, were isolated also from the blood stream. The child's condition became worse and he died on the forty-fifth day of the disease.

The bacteriology of the gram-negative micrococcus repeatedly isolated from the spinal fluid of this infant did not correspond in its reactions to that of any known organism. Details are given. Because of its luxuriant growth in all mediums tested the organism has been tentatively called *Micrococcus florens*. Tests of its virulence lead to the belief that it is pathogenic for mice, rabbits and monkeys, producing a septicemia and also, in the two latter animals, causing a purulent meningitis. The combined results of the biologic reactions and of the agglutination tests lead to the belief that the organism, though morphologically similar to the meningococcus, is yet entirely distinct.

G. Rutelli[154] describes the case of a girl, aged 6 months, admitted with symptoms of cerebrospinal meningitis. Ten c.c. of fluid obtained by lumbar puncture was turbid and formed dense white clots after a few minutes. The microscope showed numerous white cells, the neutrophil polynuclear leukocytes being prevalent, several erythroblasts and abundant filamentous organisms resembling streptothrix. An emulsion of this organism injected into the peritoneum of some white mice caused death in three days. The patient's blood did not agglutinate them. A second lumbar puncture gave identical results. Hexamethylenamin was given in doses of 1 gm. daily. The temperature continued irregular and intermittent but never rose above 38.5 C. The sequal of the case is unknown, as the parents removed the patient from the hospital.

Meyer[155] reports the case of a girl, aged 6 years, an Indian child, and her brother, aged 8 years, and sister, aged 12 years. All showed varying degrees of distinct meningeal symptoms. The first mentioned had been ill six days with headache and vomiting. Rigidity of the neck and photophobia were present. Kernig's sign was positive, the knee jerks were absent. In two of the cases trichinae larvae were found in the spinal fluid. There was marked cellular increase (lymphatic) in the spinal fluid. There was general leukocytosis and eosinophilia, 8 per cent. A clinical resemblance to poliomyelitis was noted. The finding of trichinae in the spinal fluid was first reported by Van Cett and Lintz (1914) and since then their observations have been confirmed. The presence of meningeal symptoms has not been emphasized.

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[154] Rutelli, G.: Cerebrospinal Meningitis from Streptothrix. Pediatria, 1915, **23**, 711.

[155] Meyer, J.: Trichinosis: A Report of Three Cases Simulating Meningitis, with the Findings of Trichinae Larvae in the Spinal Fluid. Jour. Am. Med. Assn., 1918, **70**, 588.

Baeslack, Bunce and co-workers[156] report the cultivation of the meningococcus from the blood. That the meningococcus occasionally gets into the blood is borne out by the occurrence of lesions in various parts of the body from which meningococci are recovered. Such a case was noted in this review last year.[157] A somewhat analagous finding is noted later (Netter, Selanier, etc.). By placing 15 or 20 c.c. of the patient's blood in each of two bottles containing from 80 to 100 c.c. of meat infusion bouillon, salt-free, to which had been added, after sterilization, 1 per cent. glucose, and 10 per cent. serum water, then incubating at 37 C., Baeslack, Bunce and co-workers have been able to obtain 36.3 per cent. positive cultures.

As the result of their study of twenty-five cases they conclude that systemic infection by the meningococcus is more frequent than previously suspected; that this systemic infection may occur without appreciable or with no meningeal localization; and that the systemic infection may be previous to, or coexistent with, meningeal involvement. Consequently, the intravenous administration of antimeningococcus serum is rational and is indicated in conjunction with the intraspinal treatment.

A second communication by Netter, Salanier, and Wolfrom,[158] a paper read before the Société de Biologie, Paris, Nov. 18, 1916, reviews the work of the last two years bearing on the recognition of meningococci in the purpuric eruptions that may accompany obvious cases of meningococcal meningitis, or precede the meningeal involvement, or even exist apart from any symptoms of meningitis whatever. These authors claim precedence. in that whereas other examinations had been made postmortem, theirs were made *during the patient's life*—a matter

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156. Baeslack, F. W., Bunce, A. H., Brunelle, G. C., Fleming, J. S., Klugh, G. F., McLean, E. H., and Salmon, A. V.: Cultivation of Meningitis Intracellularis from the Blood; Preliminary Report. Jour. Am. Med. Assn., 1918, **70,** 684.

157. Holmes, James B.: Recent Work in Anatomy, Physiology and Pathology of Childhood. Am. Jour. Dis. Child., 1917, **13,** 198.

158. Netter, A., Salanier, M., and Wolfrom: A Case of Hyperacute Purpura without Cerebrospinal Meningitis; Recognition of Its Meningococcal Nature During Life by Microscopic Examination. Brit. Jour. Child. Dis., 1917, **14,** 104.

of practical importance from a diagnostic point of view. Benda, Pick, Sharpe, Ghon and Barber are the names mentioned. They report a fresh case of primary meningococcal purpura whose nature was revealed during life by microscopic examination of the skin lesions. A 10-month-old infant had been seized with shivering and fever, followed by convulsive movements one afternoon. It was still feverish throughout the night, and next morning its mother found it had large violet spots all over the body. The child was extremely weak, dyspneic, and cyanosed, but free from signs of meningeal reaction. Lumbar puncture yielded normal spinal fluid. Scarification of the darkest purpuric patches yielded sanguinolent fluid, and in the smears of this serum were found definite and characteristic meningococci. The child died.

Miscellaneous.—Blackfan[159] reports 4 cases of lead poisoning in children. Convulsions were a prominent symptom. The knee kicks were absent; Kernig's sign was not present; the reflexes were not exaggerated. In three of the four cases, changes were found in the spinal fluid—a positive globulin reaction, or an increase in the number of cells, or both. Three of the patients died, two in the hospital and one in a succeeding attack three weeks after an uneventful recovery and discharge. The source of the lead was usually in paint gnawed from the crib or other furniture.

Stewart,[160] in 1895, reported a series of convulsions due to eating buns colored with chrome yellow. Seven of the 16 cases were in children between 1½ and 12 years of age. Numerous subsequent reports (Gibson, Love, Turner, Breinl and Young) have come from Australia where there has been an unusually good opportunity to study this condition. As Blackfan says:

> In all patients with convulsions in which the etiological factor is not clear, lead should be suspected. This can readily be determined, as in the majority of instances there are other evidences of the condition, e. g., the lead line, basophilic degeneration, and the presence of lead in the feces. The examination of the spinal fluid may prove to be an index as to the seriousness of the affection and of prognostic aid.

Several papers dealing with diseases of the muscles may be noticed: McCrudden[161] says that the myasthenia of progressive muscular dystrophy is due to hypoglycemia, and the hypoglycemia and fat deposition to impair glycogenesis, the carbohydrate of the food being probably changed largely to fat instead of glycogen. The impaired glycogenesis is due to suprarenal or other endocrine disease.

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[159] Blackfan, K. D.: Lead Poisoning in Children, with Especial Reference to Lead as a Cause for Convulsions. Am. Jour. Med. Sc., 1917, **153,** 877.

[160] Stewart: Lead Convulsions. Am. Jour. Med. Sc., 1895, **59,** 288.

[161] McCrudden, F. H.: Progressive Muscular Dystrophy. Jour. Am. Med. Assn., 1918, **70,** 1216.

This view is based on the following data: In progressive muscular dystrophy there is found a low blood sugar—and following treatment which increases the blood sugar, an improvement in muscular strength; blood sugar—glucose—is the source of energy for muscular contraction, and agencies which reduce blood sugar. Addison's disease, diphtheria toxin, and phosphorus and hydrazin poisoning, cause profound myasthenia, the severity of which is proportional to the fall in blood sugar; there is no increased utilization of sugar, shown by the absence of rise in heat formation, and no loss by the kidneys, the urine being free from sugar; there is in progressive muscular dystrophy a rapid fall in blood sugar during the first twenty-four hours of starvation—in health the normal blood sugar level is maintained during starvation—which testifies that in progressive muscular dystrophy as in all forms of experimental hypoglycemia there is a decreased rate of replenishment resulting from a diminished reserve of glycogen; the diminished glycogen reserve, in experimental hypoglycemia, results from impaired glycogen formation, the carbohydrate not being converted into glycogen, but remaining a long time in the blood, after which, judging from the amount of "fatty degeneration" in these cases, from the increased respiratory quotient, and the lipemia, it is probably changed to fat—the deposition of fat in the muscles may be so great as to lead to the use of the term hypertrophic; impaired glycogenesis may result from damage either to the liver, the organ in which glycogenesis takes place, or to the suprarvenals (or other endocrine glands), the organs that control the process; a prompt and marked rise in blood sugar following the administration of epinephrin in progressive muscular dystrophy testifies to the efficiency of the liver in the disease and points to a deficiency in epinephrin.

Reuben[162] reports six cases of amyotonia congenita (Oppenheim), and gives a full review of the literature.

Cano[163] writes of reflex amyotrophy.

Crafts[164] reports three cases of myasthenia gravis.

Navarro and Correas[165] consider the pathologic histology of the muscles in cases of severe myopathy.

Johannessen[166] writes on progressive multiple ossifying myositis.

Tuberculosis.—Clough[167] reports the cultivation of tubercle bacilli from the circulating blood of a 5-year-old colored boy suffering from miliary tuberculosis. The occurrence of tubercle bacilli in the circulating blood in miliary tuberculosis has long been recognized. The pathologic anatomy of the disease indicates that tubercle bacilli must be distributed throughout the body from a primary focus by means of the blood stream. Faber (1914) obtained a growth of tubercle bacilli on a plain agar slant inoculated with blood from the heart of a child dead of generalized tuberculosis. Clough for the first time has grown tubercle bacilli from the circulating blood of living patients. By her method positive cultures have been obtained from the blood in a relatively short time. The possibility of using the procedure in differential diagnosis is thus suggested.

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[162] Reuben, M. S.: Arch. Int. Med., 1917, **20,** 657.

[163] Cano, J. O., Rev. de med. y cirug., Havana, 1918, **23,** 59.

[164] Crafts, L. M.: Journal-Lancet, 1917, **37,** 774.

[165] Navarro, J. C., and Correas, C. A.: Semana méd., 1917, **24,** 628.

[166] Johannessen, C.: Norsk Mag. f. Lægevidensk., 1917, **78,** 839.

[167] Clough, Mildred C.: The Cultivation of Tubercle Bacilli from the Circulating Blood in Miliary Tuberculosis. Am. Rev. Tuberc., 1917, **1,** 598.

Wang and Cooley[168] have taken up the occurrence of tubercle bacilli in the breast milk of tuberculous women. Behring, in 1903, announced that pulmonary tuberculosis could result from intestinal infection and that infants often became tuberculous from the milk fed to them. Marfan mentioned two cases which he considered authentic examples of children being infected by their mother's milk and Kurashiga found tubercle bacilli in the breast milk of tuberculous women who had no mammary disease. Noeggerath was able to infect guinea-pigs with tuberculosis by injecting them intraperitoneally and subcutaneously with breast milk. He did not believe tubercle bacilli to be excreted in breast milk in large enough numbers to be a frequent and large source of danger to the child, but thought it best, nevertheless, for tuberculous mothers to feed their children artificially.

Wang and Coonley examined the breast milk of twenty-eight women. They made smears for tubercle bacilli which were negative. They injected guinea-pigs intraperitoneally with negative results. They also fed guinea-pigs the milk, thinking to see if it contained any toxic substance that might prevent thriving. Both pigs lost weight but showed no evidence of tuberculosis. With one exception, which may be questionable, the results of their studies were negative.

During recent years much work has been published tending to show the relatively great amount of infection with bovine tubercle bacilli in Edinburgh as compared with similar infection in American cities. The work of Park and Krumwiede has shown that in New York City, at least, tuberculosis in children is usually, indeed almost always, of human origin; in Edinburgh, on the contrary, a very large percentage is of bovine origin. This difference in type of infection has been attributed to the use, respectively, of pasteurized milk from tuberculin tested cows on this side and raw, less well tested milk in Scotland.

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[168] Wang, S. L., and Coonley, F.: Occurrence of Tubercle Bacilli in Breast Milk of Tuberculous Women. Jour. Am. Med. Assn., 1917, **69**, 531.

Mitchell[169] has recently published some interesting observations from Edinburgh on primary tuberculosis of the faucial tonsils obtained from children with tuberculosis of the upper cervical lymph nodes, and from children with enlarged tonsils only and without evidence of tuberculosis in the cervical glands or elsewhere.

In the first group were 100 children and 6 adults. In no case was it possible to establish the presence of tuberculosis prior to removal and examination of the tonsils (except doubtless through the von Pirquet test). The tonsils were rarely painful, and there were no symptoms except swelling of the upper cervical nodes, which in about one-fourth of the cases was slight, and in the rest rather extensive. On microscopic examination of these 106 tonsils, 41, or 38 per cent. of the tonsils were definitely tuberculous. Animal inoculations in 92 cases, yielded 20 positive results, the bovine type of bacillus being isolated in 16.

In the second group, there were 100 cases, all children with enlarged tonsils only. The cervical glands were palpable in all. Microscopically, 9 of the tonsils were tuberculous also, all 9 yielding positive results on inoculation. The type of organism was in 4 bovine, in 2 human, and in 3 undertermined.

The tubercles in the tonsils were situated near the deeper portions of the crypts, and also directly beneath the surface mucosa as well as deep in the tonsil close to the capsule, the first two being the favorite locations. The fact that the majority of the tuberculous foci were in positions within easy reach of the oral cavity suggests infection by way of the mouth. The absence of demonstrable pulmonary lesions in these cases would seem to preclude infection of the tonsils from the sputum. The high proportion of organisms of the bovine type recovered—80 per cent. in the positive inoculations in the first series and 66 per cent. of those recognized in the second series—would point strongly to the milk supply as the source of infection in primary tuberculosis of the tonsils. This work should stimulate further studies. It is to be noted that the children came from the dispensary class.

Wang[170] has studied the types of the bacilli in children at necropsy in Edinburgh. He gives the usual high bovine origin for tuberculosis in that region; 50 per cent. in children, 13 per cent. in adults; and hence concludes that it is often of intestinal origin.

Spleen and Blood.—De Lange and Schippers[171] report two cases which presented the clinical picture of splenomegaly of the Gaucher type. A study of the blood pictures presented by the brothers and sisters of the patients and their parents and grandparents left these workers with "the distinct impression that in such cases an examination of the family ought to be carried out as carefully as possible," though they would not actually state that in this instance the origin of the disease in the children could be traced back to the father. Splenectomy was successfully performed in both children. In the first child, 5½ years old, the spleen weighed 170 gm. (about five times the normal weight); in the second child, 7½ years old, the spleen weighed 470 gm. (eight times the normal weight). The splenic and lymphnodular follicles showed very great activity of the germinal centers, and karyokinetic figures in the pulp. In both spleens a number of sudanophil cells were inside and outside of the follicle. These, however, are not to be looked on as abnormal, as Kusunoki[172] found these cells regularly in his examination of 132 spleens, and according to him lipoid cells are found in the follicles of the spleen in children, whereas in adults they are seen in the pulp.

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[169] Mitchell, A. P.: Primary Tuberculosis of the Faucial Tonsils, Jour. Path. and Bact., 1917, **21,** 248.

[170] Wang: Jour. Path. and Bact., 1917, **21,** 131.

[171] De Lange, C., and Shippers, J. C.: Familial Splenomegaly. Am. Jour. Dis. Child., 1918, **15,** 249.

Though the cases presented the clinical picture of Gaucher's disease, the microscopic pictures bore no resemblance to the pathologic findings of that disease—an opinion confirmed by Dr. R. de Josselin de Jong. Apparently one had to deal with a congenital *vitium primae formationis;* on account of which the spleen developed into a state of "giant growth." And certainly one had to deal with "a familial progressive disease of the spleen which produces, sooner or later, an increasing cachexia, and in the course of which a hemorrhagic diathesis occurs antemortem."

The present status of idiopathic splenomegaly (Gaucher's Disease) is considered in a paper by Vaglio.[173]

Holsclaw[174] reports a case of acute lymphatic leukemia in a 11-month-old Japanese baby. The family history and the child's previous history were negative. She was sent into the hospital with a diagnosis of adenitis; a swelling of the glands of the neck had been noticed ten days earlier.

It was found that the mucous membranes were extremely pale, and the gums hemorrhagic. The glands were everywhere palpable. They formed a complete collar about her neck, and were hard, nonfluctuating, and discrete, not tender. The spleen was not markedly enlarged. Hemoglobin, 30 per cent.; red cells, 3,200,000; white cells, 109,000;

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[172] Kusunoki: Zieglers Beitr. z. path. Anat. u. z. allg. Path., 1914, **59.**

[173] Vaglio, R.: Present Status of Idiopathic Splenomegaly (Gaucher's Disease). Pediatria, Naples, 1917, **25,** 639.

[174] Holsclaw, F. M.: A Case of Acute Lymphatic Leukemia, with Autopsy Arch. Pediat., 1918, **35,** 151.

chiefly small lymphocytes. There was irregular fever. The child died on the nineteenth day of observation, following a transfusion. The microscopic findings were of acute lymphatic leukemia with slight infiltration of the liver and kidneys.

A case of pseudoleukemia infantum (von Jaksch's disease) with essentially negative necropsy findings is reported by Roth.[175]

Bass[176] reports a case of Winckel's disease. The combination of cyanosis, jaundice, and hemoglobinuria in the new-born is a very rare one, only about thirty cases having been recorded up to 1911 (Brandenburg), though the syndrome was first described by Parrot in 1873, and by Winckel in 1879. It is generally thought to be infectious in origin, and various micro-organisms (*B. coli,* streptococcus, pseudodiphtheria bacilli) have been claimed as the cause of the illness. The umbilicus is apparently not the portal of entry. The disease may occur epidemically in obstetric wards. Necropsy could not be obtained in Bass' case.

Lypodystrophia.—F. Parkes Weber presents two papers on Lypodystrophia Progressiva. In one[177] he reviews the published cases of this disease in females and tabulates them. He concludes that "lipodystrophia progressiva" is not always *progressive,* certainly not in regard to the extent of the area affected; that it usually commences in childhood, especially at from 6 to 8 years of age, that the disease or syndrome is not confined, as at first it was supposed, to the female sex; that the etiology is unknown, but is probably connected with a disorder of the internal secretions (endocrinic origin); and finally, that the fat atrophy, however disfiguring it may be, does not signify any danger to life, and is not usually accompanied by loss of strength and general health.

In the second paper[178] Weber reports the case of a 13-year-old English boy who was moderately fat in the face and body till the age of 8, after which loss of subcutaneous fat gradually progressed in the face and neck, and to a large extent in the arms, thorax, and abdomen. In the face, practically no fat was left save in the orbits. Ten other cases in males are tabulated; in seven, the affection appeared at from 2½ to 10 years of age. It appears that in males the fat atrophy is more often limited to the face and neck than in females.

The Severn Apartments.

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[175] Roth, David A.: Report of a Case of Pseudoleukemia Infantum (Von Jaksch's Disease). Jour. Am. Med. Assn., 1918, **70,** 1914.

[176] Bass, M. H.: Cyanosis Icterus and Hemoglobinuria in the New-Born (Winckel's Disease). Arch. Pediat., 1918, **35,** 84.

[177] Weber, F. Parkes: Lypodystrophia Progressiva. Brit. Jour. Child. Dis., 1917, **14,** 81.

[178] Weber, F. Parkes: Lypodystrophia Progressiva in a Male. Brit. Jour. Child. Dis., 1917, **14,** 179.

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